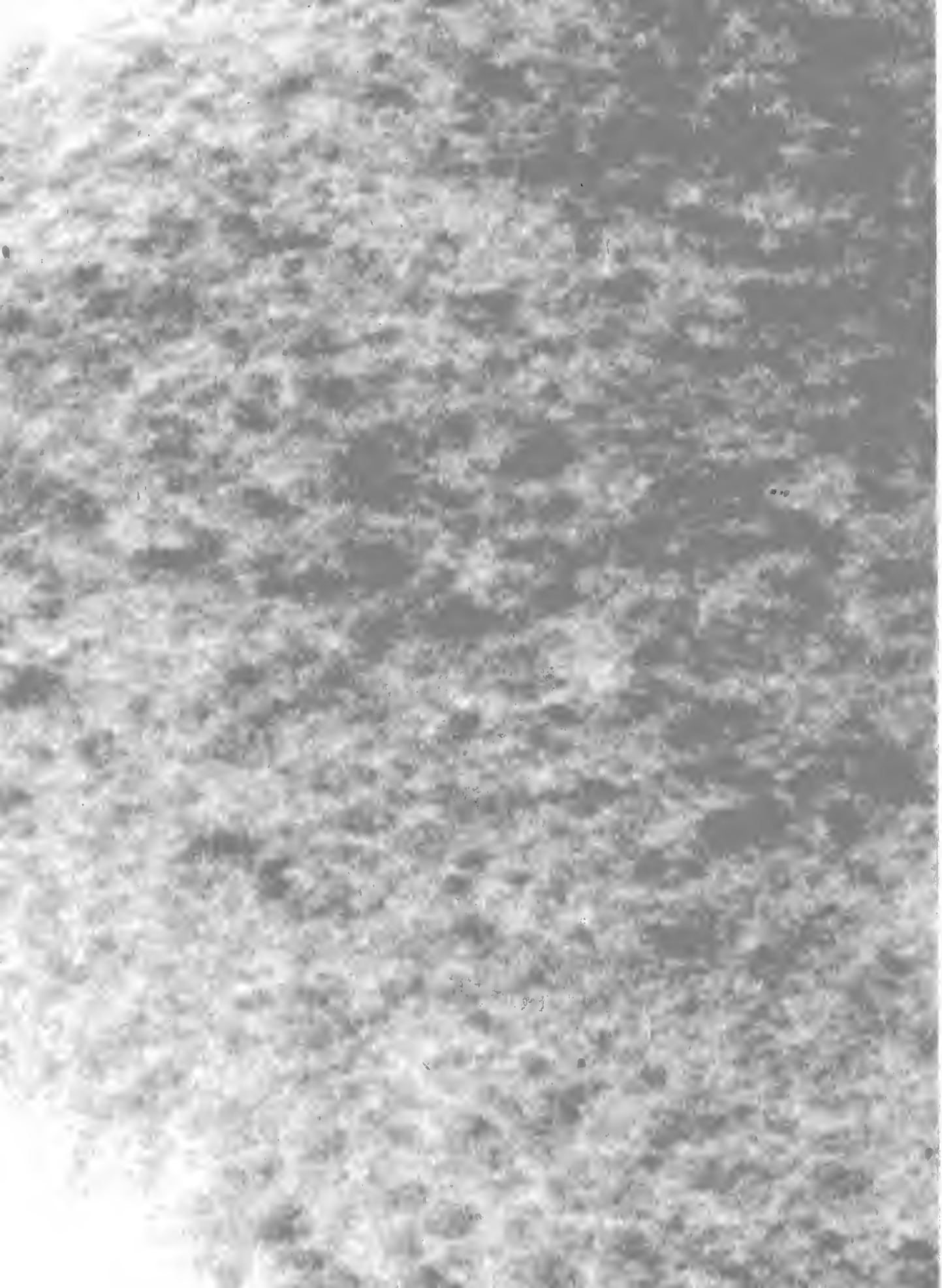
ILLINOIS--UNIVERSITY AT URBANA-CHAMPAIGN--INSTITUTIONAL REVIEW BOARD

THE USE OF HUMAN SUBJECTS IN RESEARCH AT THE UNIVERSITY OF ILLINOIS, URBANA-CHAMPAIGN



THE USE OF HUMAN SUBJECTS IN RESEARCH

AT THE

UNIVERSITY OF ILLINOIS

URBANA-CHAMPAIGN

Institutional Review Board
The Graduate College
Room 338, Administration Bldg.

AUGUST, 1976

PREFACE

Developments in the basic sciences during recent decades have made it possible to perform meaningful scientific investigations concerning living man. Sufficiently sophisticated tools have been developed and many of the necessary experiments with inanimate matter and lower life-forms have been performed. The use of human subjects in any research program, however, raises questions of ethics and propriety which rarely arise in most scientific investigations. When the number of such studies on the Urbana-Champaign campus was quite small, the University administration did not play a major role in assuring the protection of human subjects. The academic departments engaged in such work relied primarily on the professional code of ethics of the individual investigators involved.

With the increasing possibilities for scientific attention to the problems of human life in the years following World War II, it became necessary for the University to formulate more general principles for the guidance of faculty members engaged in research work with human subjects. In 1964 an ad hoc committee appointed by the Provost, consisting of F. E. Boys, M.D.; W. H. Davis, LL.M.; L. G. Humphreys, Ph.D.; O. S. Walters, M.D.; and F. Sargent, M.D., Chairman, developed such a set of general principles. These were published in a document entitled Guide to Experimental Use of Human Subjects. The responsibility for supervision remained with the department executive officers.

In the past few years, the United States Surgeon General issued policy and procedure orders and revisions which set special requirements regarding the use of human subjects in research, and the institutional review of such use, when activities were undertaken with support from the Public Health Service. More recently these additional requirements have been extended to cover work supported by any agency within the U. S. Department of Health Education and Welfare. Some other sponsoring agencies, e.g. U. S. Department of Agriculture, have adopted the DHEW regulations as well.

In 1974 continuing concern for the welfare of human subjects in biomedical and behavioral research led to the establishment of a Presidential Commission to study the ethical questions concerned and to the incorporation in the National Research Service Award Act of 1974 (Public Law 93-348) of a broader requirement for institutional review of activities involving human subjects.

The basic ethical principles developed in the mid-1960's for the use of human subjects in research on the Urbana-Champaign campus remain unchanged, but the increasing number of such activities, the specific procedural requirements of certain sponsoring agencies, and the new statutory requirements necessitate a more formalized process for overseeing of the use of human subjects on this campus.

To this end, the Institutional Review Board for the University of Illinois, Urbana-Champaign, was established in 1975, composed of John D. Anderson, Frederick C. Fliegel, W. Edward Harris, Lloyd G. Humphreys, Robert L. Sprague, Esther K. Sleator, and Willard J. Visek as Members, B. S. Katzenellenbogen, Jeffery T. Markland, and Joseph E. McGrath as Alternates and Linda S. Wilson as Executive Secretary. This Board has undertaken a review of the UIUC policy and procedures to assure their appropriateness for the nature and increased level of activities involving human subjects on this campus and to assure compliance with the various laws and regulations governing such activities.

In the pages which follow, the basic ethical considerations are reiterated, definitions are provided, the UIUC policy and procedures are set forth, and specific instructions to assist investigators in the review process are provided. In addition, the current DHEW regulations are included for reference.

All of those engaged in work involving human subjects in any component of the University of Illinois, Urbana-Champaign campus, should become familiar with and follow the definitions, instructions, policies and procedures described in this document.

Opportunities abound for research leading to significant improvement of the quality of human life, especially in a major research university such as ours. Some of this important work requires the use of human subjects. Careful attention to the responsibility for the rights and welfare of such subjects is vital both for the subjects themselves and for the freedom to continue to undertake responsible research involving human subjects.

I urge your careful study of this document.

George A. Russell
Vice Chancellor for Research and
Dean, The Graduate College

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Part I ETHICAL AND PROFESSIONAL STANDARDS FOR USE OF HUMAN SUBJECTS IN RESEARCH

The use of human subjects in research can be extremely important to the development of new knowledge in many areas. Ultimately, the only sure means for learning specifically about man is through studying man himself. Responsible investigation involving human beings as subjects, however, demands that careful attention be given to questions of ethics and propriety. The ethical and professional standards that have been widely adopted by investigators conducting studies on human beings are succinctly stated in the Nuremburg Code:[1]

"1. The voluntary consent of the human subject is absolutely essential.

2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of disease or other problem under study that the anticipated results will justify the performance of the experiment.

4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except perhaps in those experiments where experimental physicians also serve as subjects.

6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.

9. During the course of the experiment, the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

[1] Trials of War Criminals before the Nuremburg Military Tribunals. Superintendent of Documents, U. S. Government Printing Office, Washington, D.C.

10. During the course of the experiment, the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of good faith, superior skill, and careful judgment required of him, that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject."

Various professional associations have also developed and adopted ethical codes which guide investigators working in the various disciplines involved. Examples of these are:

The Declaration of Helsinki; Recommendations Guiding Doctors in Clinical Research (1964), adopted by World Medical Association. (J.A.M.A., 197 (1): 32, Sept. 12, 1966) Copies available from the American Medical Association, 535 North Dearborn Street, Chicago, Illinois 60610.

Professional Ethics - Statements and Procedures of the American Anthropological Association; September, 1973.
American Anthropological Association
1703 New Hampshire Ave., N.W.
Washington, D. C. 20009

Patients Bill of Rights, November 17, 1972
American Hospital Association, Inc.
1200 Seventeenth St., N.W.
Washington, D. C. 20036

AMA Ethical Guidelines for Clinical Investigation; November 30, 1966
American Medical Association
535 North Dearborn Street
Chicago, Illinois 60610

The Nurse in Research; ANA Guidelines on Ethical Values; January 1968
American Nurses' Association
10 Columbus Circle
New York, New York 10019

Code of Ethical Standards
American Personnel and Guidance Association
1607 New Hampshire Ave., N.W.
Washington, D. C. 20009

Ethical Principles in the Conduct of Research with Human Participants, copyright 1973

American Psychological Association, Inc.
1200 17th St., N.W.
Washington, D. C. 20036

Code of Ethics of American Sociological Association, September 1, 1971
American Sociological Association
1722 N. Street, N.W.
Washington, D. C. 20036

The Pediatric Bill of Rights, February 25, 1974
National Association of Children's Hospitals and Related Institutions, Inc.
1308 Delaware Avenue
Wilmington, Delaware 19806

NASW Code of Ethics, October 13, 1968
National Association of Social Workers
2 Park Avenue
New York, New York 10016

Ethical Standards for Research with Children
Society for Research in Child Development
University of Chicago Press
5801 Ellis Avenue
Chicago, Illinois 60637

Copies of these are available for review in the Office of the Executive Secretary of the Institutional Review Board, Room 338 Administration Building and in the University Library; copies may be obtained from the addresses given above.

The investigator using human subjects should fully familiarize himself with these ethical considerations and their implications. To this end the monographs by Beecher[2] and by Ladimer and Newman[3] are strongly recommended.

[2]H. K. Beecher, Experimentation in Man. C. C. Thomas, Springfield, Illinois, 1960.

[3]I. Ladimer, and R. W. Newman, Clinical Investigation in Medicine: Legal, Ethical, and Moral Aspects. Boston University Law-Medicine Research Institute, Boston, Massachusetts, 1963.

PART II UIUC POLICY FOR USE OF HUMAN SUBJECTS IN RESEARCH

A. Applicability

Any activity conducted at or sponsored by the University of Illinois - Urbana-Champaign which involves human subjects*, i.e. human beings whose physical, emotional, or behavioral condition, responses, tissues or fluids are investigated for any purpose other than for the sole purpose of benefitting the subject as an individual, must be reviewed.

The use of interviews, tests, observations, and inquiries designed to elicit non-public information about individuals or groups must be reviewed. However, routine course development, including evaluation of the effectiveness of such development, in courses sponsored by UIUC do not need review. Nor do non-intervening observations of public behavior, secondary use of data if the subjects are not identifiable, and use of publicly available data whether or not the subjects are identifiable.

Research projects, demonstration activities, pilot projects, student dissertation projects, independent study projects and course projects must be reviewed if they involve human subjects.

B. Statement of Policy

The University of Illinois - Urbana-Champaign affirms the need for academic freedom in the conduct of research and the value of well-designed, responsible activities which involve human subjects. At the same time it recognizes its basic responsibility to assure the protection of any human subjects so involved. To this end it has adopted the following statement of policy:

1. Investigations conducted at or sponsored by the University of Illinois - Urbana-Champaign must adhere to the principles set forth in the Nuremburg Code, or one of the ethical codes developed by the various professional associations, and must adhere to the policies and procedures set forth in this document.

2. Participation of human beings as subjects in research* governed by this policy must be voluntary, i.e. it must occur as the result of free choice without compulsion or obligation. Both the rights of such individuals to be protected against injury or invasions of their privacy, and their interests as members of a free society in preserving their dignity, are recognized as of major concern and must be protected.

   Where minors, mentally retarded or mentally disabled persons, individuals with limited civil freedom, pregnant women, fetuses, children, or the dead are subjects in an investigation, special care must be taken to assure that consent* for participation is obtained from authorized representatives in accordance with applicable statutes and regulations.

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* See page 5, Section II C for definition and discussion of the terms research, subject, risk, and consent.

3. Projects involving human subjects should be carefully designed to minimize risk* to the subjects. As far as possible, any risk should be anticipated in advance. Proper precautions should be taken and plans made to deal with emergencies that may develop in the course of even seemingly routine activities.

4. Methods of approaching subjects and securing their participation must be disclosed in the description of the project submitted for review by the Institutional Review Board or department executive officer. No coercion, explicit or implicit, should be used to obtain or maintain cooperation.

5. Any payment made to subjects should not be large enough to constitute excessive inducement for participation of subjects. Plans for payment of subjects must be disclosed in the description of the project submitted for review by the Institutional Review Board or department executive officer.

The UIUC process for prior review, and timely periodic review after approval, of research, development and related activities involving human subjects is for the purpose of assuring independent determination whether the subjects will be placed at risk, and, if risk is involved, whether:

(a) any risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the project to be undertaken;

(b) the welfare of any such subjects will be adequately protected; and

(c) legally effective informed consent will be obtained by adequate and appropriate methods.

C. Definition of Terms

1. Research

Human beings may be studied in many ways and under a vast variety of circumstances and conditions. For these reasons the word "research" is elusive and difficult to define with precision. On the one hand, research may be used to describe something as innocuous as a new approach to teaching or the questions in a public opinion survey. It is also recognized that the subject may be exposed to the gravest mortal risks, such as the astronaut who prepares to be launched into space, to orbit the earth, or journey to the moon. As used in this document, the word research is defined as a trial or special observation, usually made under conditions determined by the investigator, which aims to test a hypothesis, to discover some unknown principle or effect, or to illustrate some known or suggested truth. The term research is intended to apply to systematic studies in which any substance or stimulus is administered to a subject by any

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* See page 5, Section II C for definition and discussion of the terms research, subject, risk, and consent.

route. It is intended to apply to studies which involve changes in physical or psychological state or environment or major changes in diet and to the pertinent methods for studying alterations in body functions and behavior under such conditions. It is intended to apply to the use of interviews, tests, observations and inquiries designed to elicit nonpublic information about individuals or groups.

It is not intended to apply to routine course development, including evaluation of the effectiveness of such development, in courses sponsored by the University of Illinois. Nor is it intended to apply to non-intervening observation of public behavior, secondary use of data if the subjects are non-identifiable, or use of publicly available data whether or not the subjects are identifiable.

2. Subject

There are several types of human subjects. For example, the subject may be an adult, a minor, a student, a hospitalized patient, a client, a resident of an institution for the mentally ill or retarded, a prison inmate, etc. Donors of organs, tissues, body fluids and services, and informants are also considered to be subjects. It is useful to distinguish between normal subjects and those which are of interest because of an illness or dysfunction they exhibit. A subject is considered to be a "normal" subject if his/her participation in the research is not determined by any illness or dysfunction that he/she exhibits and if his/her health cannot be foreseen to benefit by participating in the research. Hospitalized patients volunteering to participate in research that bears no relationship to their illness or its treatment may be regarded by the investigator as "normal volunteers."

Of particular concern are the following types of subjects:

a) Subjects with limited civil freedom, such as prisoners, residents or clients of institutions for the mentally ill and mentally retarded, and persons subject to military discipline.

b) Pregnant women, the viable fetus (both in utero and ex utero), the newborn, children, minors and the dead. (the unborn and the dead should be considered subjects to the extent that they have rights that can be exercised by their next of kin or legally authorized representative.)

The definition of subject excludes all accepted and established service relationships, such as the normal relationship of patients to physicians, students to professors, and other clients to professionals in which the patient, student or client is receiving aid or services consistent with accepted and established practice, and intended only to meet his own personal needs. The professional-client relationship has the welfare of the client as the primary objective, whereas the investigator-subject relationship has the discovery of new knowledge as its primary objective. This difference may not be fully understood by the subject who is also a client, and can result in the investigator's gaining consent without free decision, in part due to a trust based on a presumed role which the investigator is not necessarily fulfilling at that time.

The normal employee-employer relationship, in which legitimate services are rendered for salary, wages or remuneration in keeping with customary written or verbal contracts, is also excluded from the definition of subject.* If doubt exists as to whether the procedures to be employed are within accepted and established practice or as to whether the purpose is only for the personal needs of the client, the activity should be considered to involve subjects whose rights and welfare are to be protected in accord with this policy statement. Similarly, if doubt exists as to whether the procedures are within the normal limits of the employee's work scope, employees should be considered to be participating as human subjects, and their rights and welfare must be protected.

3. Types of Risks

There are different risks inherent in different research procedures.

Risk is most obvious in medical and behavioral science research projects involving procedures which may induce a potentially harmful altered physical state or condition: surgical and biopsy procedures; the removal of organs or tissues for study, reference, transplantation, or banking; the administration of drugs or radiation; the use of indwelling catheters or electrodes; the requirement of strenuous physical exertion; subjection to deceit, public embarrassment, and humiliation.

There is a wide range of medical, social, and behavioral projects and activities in which no immediate physical risk to the subject is involved, e.g., those involving the use of personality inventories, interviews, questionnaires, observation, photographs, taped records, and stored data. However, some of these procedures may involve varying degrees of discomfort, harassment, invasion of privacy, or may constitute a threat to the subject's dignity through the imposition of demeaning conditions.

There are also medical and biomedical projects concerned solely with organs, tissues, body fluids, and other materials obtained in the course of routine performance of medical services such as diagnosis, treatment and care, or an autopsy. The use of these materials obviously involves no element of physical risk to the subject. However, their use for many research, training, and service purposes may present psychological, social, or legal risks to the subject. In these cases, review is necessary to determine that the circumstances under which the materials were procured were appropriate and that adequate and appropriate consent was, or can be, obtained for the use of these materials for project purposes.

Some studies depend upon stored data or information which was obtained for different purposes.

a) If the material to be used in the research involves identifiable subjects, the review of the risk involved must include a determination of whether the use of these materials is within the scope of the original consent, whether consent is necessary, and whether it can be obtained.

b) If the material to be used in the research does not involve identifiable subjects, no review is necessary.

*Payment of subjects does not alter their status as subjects.

Certain risks are inherent in life itself, at the time and in the places where life runs its course. Risks of everyday living include the ordinary risks of public or private living; those risks associated with admission to a school or hospital; and the risk inherent in professional practice, as long as these do not exceed the bounds of established and accepted procedures, including innovative practices applied in the interest of the individual patient, student, or client.

Any activities which expose the subject to significant physical risk require special consideration. The investigator and those who review his plans should carefully weigh whether supervision of a physician is advisable. In cases where a physician's supervision or availability is deemed advisable, the individual investigator shall have the responsibility to make the necessary arrangements to provide for it. The fact that some types of experimentation do not involve risks beyond those experienced in ordinary life situations does not mean that the investigator is any less responsible for his/her subjects.

4. Informed Consent

The ethical and professional codes governing the use of human subjects in research provide that no research involving human subjects as governed by this document should be undertaken without the voluntary consent of the human subject, or from his/her authorized representative if the subject lacks the capacity to consent.

When the research does not place the subjects at risk, there is no single method required to assure that the subject consents to participation. The subject's consent may, for example, be secured via a written document, it may be obtained orally, it may be implicit in voluntary participation in a well-advertised activity. However the subject's consent is obtained, it must be "informed" consent, i.e., the knowing consent of an individual or his/her legally authorized representative, so situated as to be able to exercise free power of choice without the presence of excessive inducement or any element of force, fraud, deceit, duress, or other form of restraint or coercion.

A dilemma arises because in some research, fully informing the subjects would invalidate the experiment. If it is necessary to withhold information from the subject, the investigator must carefully inform the reviewers of what information will be withheld from the subjects and must clearly justify the withholding of information. Debriefing procedures to be used must also be described to reviewers. The reviewers must then decide whether the justification is sufficient and whether the subjects' rights and welfare are adequately protected. Nondisclosure of information to subjects must not be used simply to assure their participation in the research.

Investigators proposing to place any subject at risk are obligated to obtain legally effective informed consent. The basic elements of information necessary to such consent include:

(i) A fair explanation of the procedures to be followed, and their purposes, including identification of any procedures which are experimental;

(ii) A description of any attendant discomforts and risks reasonably to be expected;

(iii) A description of any benefits reasonably to be expected;

(iv) A disclosure of any appropriate alternative procedures that might be advantageous for the subject;

(v) An offer to answer any inquiries concerning the procedures; and

(vi) An instruction that the individual is free to withdraw his consent and to discontinue participation in the project or activity at any time without prejudice to the subject.

It is best to use a written document in obtaining the consent of subjects to be placed at risk. Whether the consent is obtained via a written document or is obtained orally, it must include all of the basic elements of informed consent described above and some documentation of consent must be kept in the investigator's records. The use of methods other than a written document is sometimes more appropriate. In such cases, the method to be used must be described and justified in the material submitted for review. Occasionally, fully informed consent may itself have injurious effects on the subject, or it may invalidate the experiment, as in the use of placeboes or double blind studies. If information is to be withheld from the subject, the investigator must inform the reviewers what information will be withheld from the subjects, justify the withholding of information, and describe any debriefing procedures to be followed. The reviewers must consider this information and decide whether the withholding of information is justified and whether the subjects' rights and welfare are adequately protected. Nondisclosure of information must not be used to secure the participation of subjects.

Note: However informed consent is obtained, and whether or not subjects will be placed at risk, no exculpatory language may be included through which the subject is made to waive, or appear to waive, any of his/her legal rights, including any release of the University or its agents from liability or negligence.

Note: Special procedures for obtaining and documenting informed consent of subjects placed at risk in activities supported by DHEW and certain other sponsoring agencies. See Appendix D, Sections 46.9 and 46.10 for these requirements.

Appendix A contains samples of basic informed consent documents and instructions for their use. It should be realized that the consent form is not a release. As mentioned above, it must not contain exculpatory language. The signed consent form is simply evidence of disclosure of essential information necessary to obtain an informed consent.

5. Confidentiality of Data

Both the rights of the subjects to be protected against injury or illegal invasions of their privacy and their interests as members of a free society in preserving their dignity, are recognized as of major concern and must be protected. The more sensitive the material, the greater the care that must be exercised in obtaining, handling and storing data. Provisions relating to the degree and kind of confidentiality of data and anonymity of the subjects must be specified in the description of the project submitted for review. Ordinarily, the following requirements must be met, subject only to their appropriateness to the particular activity:

a. Questionnaires, inventories, interview schedules, and other data gathering instruments and procedures should be carefully designed to limit the personal information to be acquired to that absolutely essential to the activity.

b. Data that include information which would reveal a subject's identity should be stored in files accessible only to the project investigator and his/her authorized staff or representatives.

c. As early as feasible, the data should be handled in coded form, i.e., the subject's name and information that would reveal his/her identity should be removed. Plans for the ultimate disposition of the data should be made.

d. The identity of subjects must not be released except with their express permission.

e. Use of stored data or information originally obtained for different purposes which involves identifiable subjects, requires examination of the risk involved, a determination of whether the new use is within the scope of the original consent or whether obtaining additional consent is necessary and feasible, and provision for the preservation of anonymity of the subjects.

Data that are part of the public domain are not covered by the foregoing restrictions.

D. Classification of Circumstances Involving Human Subjects

Human subjects at the University of Illinois participate in a great variety of experimental circumstances ranging from classroom demonstrations where there are no risks beyond those associated with customary work-a-day existence to experimental studies of drugs, vaccines, radioactive materials, and severe physiological stresses where there is a definite risk. For the purposes of safeguarding the human volunteers and assuring that these safeguards are continuously provided, the circumstances where human subjects are used may be grouped into two categories:

1. Subjects engage in activities with customary everyday risks.

2. Subjects engage in activities where the risk is greater than that encountered in ordinary conditions and customary activities. All research protocols that involve procedures that may induce potentially harmful, altered psychological or physical states or conditions, untried diagnostic and surgical procedures or devices, biopsy procedures, removal of organs or tissues for study, reference, transplantation or banking, administration of drugs or radiation, use of in-dwelling catheters or in-dwelling electrodes, and procedures which require strenuous physical exertion, fall in this category.

Several examples of uses of human subjects are cited in Tables 1 and 2, pages 12 and 13, where the circumstances are classified according to these two categories. These examples, which are merely illustrative, should serve as guides for the classification of future studies involving human subjects. In classifying research involving human subjects, the investigator and those who review the proposed use of subjects, should not simply attempt to identify the research with these examples, but should follow the principles and procedures of this document in arriving at a carefully reasoned decision.

The two categories of activities involving human subjects described above require different safeguards for the rights and welfare of the subjects. Investigators, deans, directors, and department heads are responsible for assuring that these safeguards are provided accordingly.

Category 1 Activities involving risks of ordinary life
(Subjects considered to be "not at risk")

1. Participation must be voluntary, but signed, written consent forms are not required.

2. All volunteer subjects should be able to state that they have no disorder or defect contraindicating their participation in the proposed project.

3. The project must be supervised by a qualified faculty or staff member.

Category 2 Activities involving risks greater than those of ordinary life
(Subjects considered to be "at risk")

1. Participation must be voluntary and signed written consent forms are considered mandatory, unless another method for obtaining consent is specifically approved by the IRB.

2. A written record of the experiments detailing the procedures employed and the results obtained shall be made and kept for reference.

3. The project must be supervised by a qualified faculty or staff member.

4. When the risk involved is a significant physical risk, the investigator and those who review his/her plans must determine:

   a) Whether it will be necessary for the subjects' physical condition to be evaluated by a licensed physician who is acquainted with the possible hazards of the proposed investigations;

   b) Whether supervision or ready availability of a physician is advisable for the project.

5. No form of radioactive material may be experimentally administered to human volunteers without the authorization of the persons responsible to the University for the appropriate and safe use of radioactive materials.

6. No Investigational New Drugs (drugs not certified by FDA for clinical use) may be administered without compliance with the FDA requirements, which include appropriate notification to FDA and receipt of either a waiver or permission (and an IND number).

NOTE: Where human experimentation forms an integral part of the conduct of a course of instruction, the official University bulletins and timetables should state the fact in the description of the course. A statement such as "Includes limited voluntary participation as a subject in experiments" should be a part of the course description. This statement would serve to alert registrants of this characteristic of the course, but would not suffice as the only means of assuring that the subjects' participation in individual experiments is voluntary. Care must be exercised to assure the absence of coercion, either real or perceived, in utilizing students as subjects.

Table 1. Examples of Research in Category 1

1. Studies of the psychological and physiological effects of mild to moderate sleep loss.

2. Studies of movement and moderate exercise of asymptomatic children and young adults where adverse effects are not anticipated.

3. Classroom demonstrations and experiments on physiological responses to moderate exercise, mild thermal stress, breathing atmospheres with slightly reduced oxygen or slightly elevated carbon dioxide, etc.

4. Most psychological studies of learning, conditioning, sensory perception, personality, and group situations.

5. Psychological and judgment responses to speech.
6. Psycho-social studies of childhood obesity.
7. Behavioral studies of child development.
8. Corrective therapeutic exercise.
9. Industrial work studies with mild to moderate work load and mild to moderate thermal stress.
10. Clothing and textile studies under conditions of mild to moderate thermal stress.
11. Psychological studies of hypnosis where the subjects are not subjected to physiological or emotional stress. In this context the volunteer under hypnosis will not be asked personal questions which relate to his private life.
12. Nutritional studies in which the subjects are expected to ingest neither unusual diets nor diets which are deficient in essential nutrients
13. Taste panel studies and taste tests.

Table 2. Examples of Research in Category 2

1. Simulated high altitude flights.
2. Psychological studies of hypnosis where subjects are subjected to physiological or emotional stress.
3. Adult exercise and fitness testing where the imposed work load exceeds by about 200 per cent the customary work of the individual.
4. Industrial work studies where there is hard physical work and high environmental temperature.
5. Physiological studies of sweating involving special nutrient regimens, dehydration, and work in thermally stressful surroundings.
6. Pharmacological studies of prescribed drugs.
7. Studies of cold viruses, vaccines, and antibiotics.
8. Studies of prescribed tranquilizer drugs on driving skills.

Part III ADMINISTRATION OF STANDARDS AND SAFEGUARDS

A. The UIUC Institutional Review Board

1. Origin of the IRB

The long established UIUC principles for responsible use of human subjects in experimentation were originally administered in a totally decentralized manner consistent with the relatively low level of such activities and the decentralized nature of the institution. Later small review committees selected from a roster of informed and competent professionals in appropriate disciplines, supplemented the departmental review of activities involving human subjects sponsored by the Public Health Service, or the U. S. Department of Agriculture. The increase in the level of such activities and the increasing specificity of sponsoring agencies' regulations led to the establishment of a single Institutional Review Board in the Fall of 1975.

2. Composition of the IRB, and Selection of its Members

The UIUC Institutional Review Board consists of at least five members, two of whom are licensed to practice medicine, two of whom have competence in the behavioral sciences or related specialties, such as anthropology, psychiatry, psychology, and sociology, and and at least one of whom is not an employee of the University of Illinois. Each member has a designated Alternate. Members of the Board and their Alternates are appointed by the Vice Chancellor for Research for specified overlapping terms so that continuity and experience is assured. Information on the current composition of the Board may be obtained from the Executive Secretary of the Institutional Review Board.

3. Meetings of the IRB

The IRB meets regularly, normally at least monthly, to review proposed and continuing activities involving human subjects and to carry out its various responsibilities, as described later in this document. The quorum is defined to be a simple majority of the number of Members of the IRB. Alternates may serve for Members in their absence, are invited to attend all meetings of the Board, and are kept well informed concerning the Board's policies and procedures, and the applicable laws and regulations. No member or Alternate shall be involved in either the initial or continuing review of an activity in which he/she has a conflicting interest, except to provide information requested by the Board.

4. Role of the IRB

The Institutional Review Board serves as the primary locus of institutional authority and responsibility for activities involving the use of human subjects. Its responsibilities include:

(a) Development of policy and procedures for review of such activities

(b) Development of information and instructions for investigators, reviewers and subjects involved with such activities

(c) Initial and continuing review of such activities

(d) Documentation of review of such activities in conformity with applicable law, regulations and policies

(e) Provision of advice and counsel to investigators engaged in such activities

(f) Adjudication of differences and review of problems arising out of such activities

As such it serves the needs of a large complex institution and satisfies the DHEW regulations which require that any institution undertaking DHEW supported research, development and related activities in which human subjects are involved must provide certain assurances, meet certain standards and establish an Institutional Review Board to conduct initial and continuing reviews of such activities in accordance with the regulations. It satisfies the regulations of the USDA and various other federal and non-federal agencies which require adherence to the DHEW regulations on protection of human subjects. And it also satisfies the broader requirement of the National Research Service Award Act of 1974 (Public Law 93-348) which stipulates that any entity which applies for a DHEW grant or contract to support a project must establish an Institutional Review Board to review biomedical and behavioral research conducted at or sponsored by such entity in order to protect the rights of the human subjects.

B. Responsibility for Compliance with Ethical Standards and UIUC Policy

The ethical and professional standards governing the use of human subjects in experimentation are described in Part I of this document. Part II set forth the University's policy in these matters and provided definitions of commonly used terms. The responsibility for compliance with these standards and the UIUC policy lies as follows:

a) The responsibility to initiate the review process and the responsibility for day to day assurance of protection of the rights and welfare of human subjects both lie with the individual(s) responsible for the conduct of the activity, i.e., the project or program director, principal investigator, fellow, trainee, or student undertaking the activity.

b) If the individual responsible for conduct of the activity is not a UIUC employee or student, but is obtaining access to subjects through the UIUC, the individual providing access to the subjects is responsible to assure that UIUC guidelines, including review, are met.

c) The responsibility for the initial and continuing reviews must fall also on persons both knowledgeable about the University's policy and relevant regulations and in a position to make an independent, objective determination that the activity is consistent with the University's Guidelines, i.e., with the departmental executive officer, the Institutional Review Board and its Advisory Committees.

Many UIUC activities involve interaction between an "investigator" and human beings. For some of these activities the responsibility for appropriate review and supervision to assure that the rights and welfare of the human beings involved are protected, has already been established. Duplicative review by the Institutional Review Board would serve no useful purpose. For some activities the nature of the activities is such that individual review is unnecessary and only the criteria by which review of such activities is judged unnecessary needs review by the IRB. For still others, the nature of the activities is such that individual review is necessary. Guidelines are therefore necessary for deciding which UIUC activities fall within each of these categories.

Section C (below) presents the guidelines for deciding whether and what kind of Institutional Review Board review is required. Section D (below) presents the specific review procedures to be followed for the various categories of activities involving human subjects. Appendix E provides Instructions for Investigators.

NOTE: Anyone conducting a study using human subjects which has not been reviewed and approved as specified herein is in violation of University policy and the applicable laws and regulations.

C. Guidelines for Determining Whether and What Kind of IRB Review is Required

1. Activities involving human beings which do not require Institutional Review Board review.

The following types of activities already have an established assignment of review and supervision adequate to assure that the rights and welfare of the human beings are protected:

Type of Activity	Responsibility
a. Projects undertaken by faculty or administration involving student or employee records.	University policy restricts access to student and employee records. Specific individuals have been assigned responsibility for assuring privacy, and guidelines have been set for determining who may gain access, under what conditions and for what purposes.
b. Accepted and established service relationships (such as the normal relationship of patients to physicians students to professors, and other clients to professionals) in which the patient, student or client is receiving aid or services intended only to meet his/her own personal needs. The normal employer-employee relationship in which legitimate services are rendered for salary, wages, or remuneration in keeping with customary written or verbal contracts, except of course when the purpose of employment is service as a subject. Payment of subjects does not alter their status as subjects. It should be noted that any of the relationships can be converted into an investigator-subject relationship if the client's benefit and welfare is not the overriding purpose of the service performed, or if the procedures are not within the normal limits of the employee's work scope. In such instances, the activity would need to be reviewed by the Institutional Review Board and would fall in either category 2 or 3 described below.	Professional and ethical codes govern these relationships. Training in the professions is supervised by professionals who have the responsibility to assure protection of rights and welfare of clients involved.

2. Activities involving human subjects which require Institutional Review Board review collectively, but not individually.

A large number of activities involving human subjects at no risk beyond those of ordinary life are undertaken each year without external funding. Some are, for example, part of introductory and research methods courses; some are short term pilot projects, doctoral dissertations and independent study projects. Some are regular faculty research projects. Some involve new use of previously gathered data on human subjects.

The large volume of such activities, the fact that for most of these, any risks to the human subjects fall well within the risks of ordinary life, and the fact that for many the time available for review is extremely short, dictate that review be expeditious and simple as well as responsible.

Review of such activities may be handled by the establishment of departmental guidelines on the basis of the recurring types of "ordinary risk" activities undertaken by the department and the well established and accepted professional procedures used in the department. When such Guidelines have been approved by the Institutional Review Board, activities involving human subjects, which are not externally funded, and which fall within the Guidelines, would not need to be reviewed individually by the IRB.

Departments wishing to use this review mechanism must submit written guidelines to the IRB which will review them to be sure that the IRB's responsibilities can be fulfilled. Appendix B of this document sets forth specific requirements for the content of departmental guidelines.

The review procedure for activities in this category is described in Section D 2 below.

3. Research involving human subjects which require Institutional Review Board review.

The following types of activities require Institutional Review Board review:

a. Research which is carried out without external support and which does not fall within departmental guidelines approved by IRB.

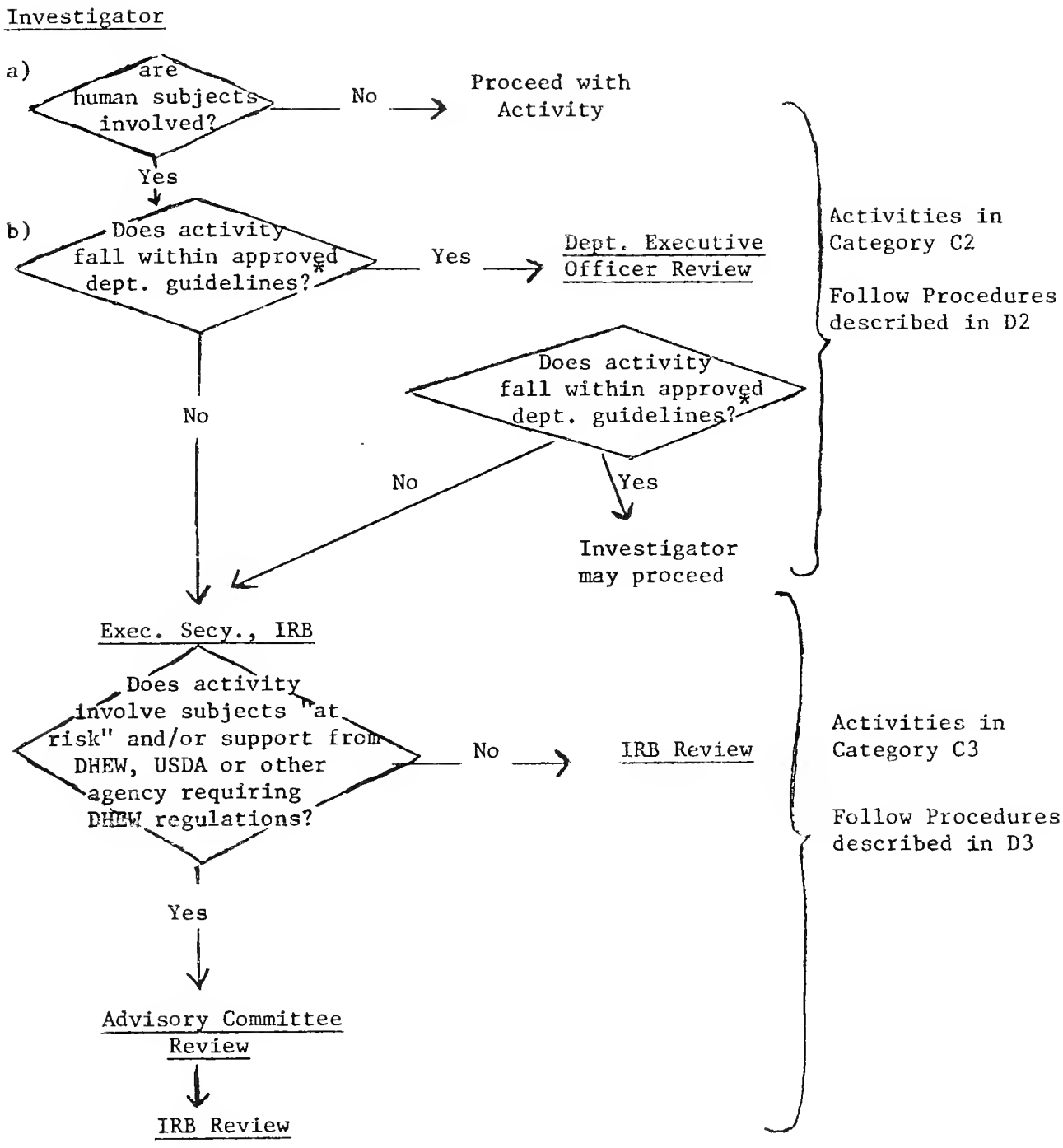
b. Research activities supported by, or proposed for support from, external sponsors.

c. Any activities which do not require IRB review, but for which IRB review is requested by the investigator or the institution.

The review procedure for activities in this category are described in Section D 3 below.

D. Review Procedures

1. Summary of the Review Path Alternatives



*NOTE: Externally funded activities and activities involving subjects "at risk" by definition do not fall within approved departmental guidelines.

2. Procedures for activities which fall within departmental guidelines approved by IRB.

a. All activities involving human subjects must be supervised by competent staff members.

b. Before any project using human subjects can be initiated, the investigator, or in the case of a student project, the supervising staff member, must provide to the executive officer of his/her unit a description of the proposed activity including:

i) description of subjects to be used and how they will be obtained

ii) description of the planned use of human subjects

iii) description of the risks involved and benefits to be obtained

iv) description of the procedures to insure protection of the human subjects, including the methods to be used to assure informed consent and confidentiality of data.

For detailed instructions see Appendix E, Instructions for Investigators

c. The executive officer, or the individual(s) designated by him/her to carry out this function, will review the proposed activity to insure that it is in accordance with the departmental guidelines approved by the Institutional Review Board. If he/she finds that the project does not comply with the IRB approved departmental guidelines, he/she will inform the investigator that IRB review is necessary and that no work with human subjects may take place until the proposed activity has received IRB approval.

At his/her discretion the executive officer may also request IRB review of projects which do fall within IRB approved departmental guidelines.

The formality with which the departmental review will be conducted will be left to the discretion of the unit executive officer. At his/her option, "Information for Review of Activity Involving Human Subjects" (Form IRB-1, See Appendix C), with attachments may be used to provide information for review.

NOTE: If the proposed activity will be undertaken or supervised by the unit executive officer, the description of the proposed project must be forwarded to the Secretary of the Institutional Review Board who will undertake the review normally carried out by the unit executive officer.

d. If the unit executive officer refuses to approve a project proposed by a Responsible Project Investigator, and the RPI believes the study is in conformity with university policy regarding the use of human subjects, the RPI may appeal that decision directly to the Institutional Review Board. The IRB will then conduct a review of the proposed study and render a decision.

e. The nature of the documentation of the departmental reviews is left to the discretion of the unit executive officer, but must be sufficient for reports to be made to the IRB on the department's experience with this procedure.

f. The investigator is responsible for insuring that the procedures are carried out as approved, for requesting another review by his/her unit executive officer if significant changes in procedure are needed, for requesting annual reviews of projects which continue longer than one year, and for notifying the unit executive officer if any problems arise involving human subjects.

g. The unit executive officer is responsible for conducting further reviews if changes are proposed, for up-dating reviews of projects continuing longer than one year, and for notifying the Institutional Review Board of any problems which arise involving human subjects.

3. Procedures for Activities which do not fall within the IRB approved departmental guidelines and for activities which are supported by, or proposed for support by external sponsors.

a. These procedures cover all such projects done at the University or under the auspices of the University. Thus projects carried out by the faculty, students or staff, projects done as theses or dissertations, projects done as part of a course or independent study, are all included regardless of the type of sponsored agreement (i.e., research grant, contract, training grant, fellowship, research career development award, etc.) involved if externally funded.

b. Before any such research, development or related activity can be reviewed and approved, it must have associated with it a Responsible Project Investigator (RPI) who is a qualified faculty member at or above the level of instructor or qualified staff member and who will monitor the conduct of the activity.

c. Before any project using human subjects can be initiated the faculty or staff member who is the Responsible Project Investigator (RPI) must submit to the Executive Secretary of the IRB eleven (11) copies of Form IRB-1 ("Information for Review of Activity Involving Human Subjects," see Appendix C) with appropriate attachments providing the protocol of the planned use of human subjects, description of the subjects to be used and the method to be used to obtain them, a description of the inherent risks and benefits involved, if any, and a description of the procedures which will be followed to insure the protection of the human subjects, including the methods to be used to assure informed consent and confidentiality of data.

For detailed instructions, see Appendix E Instructions for Investigators.

If the project is being proposed for external support, the IRB-1 forms and attachments should be submitted to the Secretary of the IRB well in advance of the deadline for submission of the application to the sponsor, and certainly no later than simultaneously with submission of the application for review through the campus administrative channels. Advance submission gives the investigator the benefit of review prior to the preparation of the final form of the application, thus insuring that any procedural revisions required by the IRB will not delay submission.

d. Before approving the Proposal Transmittal Form* attached to proposals to external sponsors, the unit executive officer will check to see whether the project involves human subjects and that the form is properly marked with regard to the use of human subjects.

e. The Secretary of the University Research Board, and others designated by the Chairman of the Research Board, who review for the Board all proposals submitted to external agencies will check each proposal to make sure that those which involve the use of human subjects are identified.

f. The Institutional Review Board will review all such projects. At its discretion the Institutional Review Board may seek the advice of members of one or more of the Advisory Committees established for this purpose. The Institutional Review Board will normally seek such advice on all projects in which the subjects are "at risk" and for projects to be undertaken with DHEW or USDA support. The Board may accept or reject the advice of the Advisory Committee members in taking its action on a proposed activity.

*The Proposal Transmittal Form is the internal form which accompanies each proposal for external support as it is routed through campus administration channels.

g. The Secretary of the IRB will inform the investigator, the department, and the sponsor if required, of the action of the IRB. In notifying an investigator of approval by the IRB, the Secretary informs the investigator of any special requirements set by the IRB. The notification will also state again the requirements for prior review of any changes in procedures involving human subjects and for additional review as stipulated by the IRB (at least annual review is required).

Within eight months of the notification of approval, the Secretary of IRB will again notify the investigator of the need to keep the IRB informed of his/her plans, including any changes in procedures, so that a new review can be made within one year from the current IRB approval and so that any application for extension or continuation of support can be considered by the IRB well in advance of its effective date. Where more frequent than annual review is deemed advisable by the IRB, the investigator will be so informed and the follow-up procedures will be adjusted accordingly.

h. The Responsible Project Investigator is responsible for insuring that the procedures are carried out as approved, for requesting another review if significant changes in procedure are needed, for requesting annual reviews of any projects which continue longer than one year, and for notifying the unit executive officer if any problems arise involving human subjects.

i. The unit executive officer is responsible for notifying the IRB of any problems which arise involving human subjects.

E. Special Procedures for Applications and Proposals Lacking Definite Plans for Involvement of Human Subjects

Certain types of activities are planned and initiated with the knowledge that human subjects will be involved in the project, but without definite plans for protocols to be followed. Examples of such proposed activities are:

1) training programs in which individual training projects remain to be selected or designed;

2) research, pilot, or developmental studies in which the involvement of human subjects depends upon such things as the completion of survey instruments, prior animal studies, or the purification of compounds.

3) general support programs where selection of the project is the responsibility of the institution or administrator of the program rather than the funding agency.

Such proposed activities will be reviewed initially in the same way as are activities with fully developed plans, but additional review will be required when the plans are fully designed. It is the investigator's responsibility to submit the plans for review when they are developed. No work involving human subjects may proceed without prior review of the procedure to be followed.

In activities supported by DHEW, a separate certification must be submitted to DHEW for each project for which plans for the use of human subjects are completed after the initial review.

In some activities of this type, the number of separate projects is large, the number of different protocols involving human subjects is small, and the subjects involved are not at risk. To facilitate responsible review of such individual projects under externally funded programs, the IRB delegates to the unit executive officer the responsibility to review the individual projects if the following conditions are met:

a) The protocol for use of human subjects has been reviewed and approved by the IRB within the year.

b) The nature of the subject population to be used does not alter the classification of "not at risk."

If these conditions are not met, the project must be individually reviewed by the IRB.

When the unit executive officer performs this review for the IRB, he/she will provide the following information to the Executive Secretary of the IRB for each such project:

a) Name of project director (and responsible faculty supervisor, if project director is not a faculty member)

b) Identification of protocol to be used, indicating name of investigator for whom it was reviewed and approved by IRB

c) Title of project to be undertaken

d) Name of external sponsoring agency and identifying number of grant or contract

e) If activity is sponsored by DHEW, a DHEW form 596 (copies available from Executive Secretary of the IRB) completed through item 3.

F. Special Procedures to be Used When Access to Subjects is Gained through a Cooperating Institution.

Investigators at UIUC may gain access to subjects through cooperating institutions. For example, a UIUC investigator may arrange with a physician at a local hospital to obtain surgical tissue or body fluid taken from the donor for therapeutic or diagnostic purposes. Where the identity of the donor remains unknown to the investigator, the physician obtains the patient's written consent for the procedure including the use of such material for study (as covered in the uniform anatomical gift act), and there is no risk to the donor, no special procedures are required. However, UIUC investigators should make sure that an authorized official of the cooperating institution is informed of the cooperative arrangement. Another example which occurs frequently on the UIUC campus is the use of school children as subjects. Here again, the investigator should always make sure that the authorized school officials are informed of the project. If the subjects are at risk, the consent of the subject's parent or guardian is required.

In any situations in which subjects at a cooperating institution will be placed at risk, the following information must be submitted to the IRB for review:

INSTITUTIONAL AUTHORIZATION FOR ACCESS TO SUBJECTS

Status of Subjects: ☐ Wards ☐ Residents ☐ Employees

☐ Patients ☐ Students ☐ Other (explain)

Number of Subjects: _____ Age Range of Subjects: _____

Name & Address of Cooperating Institution _____

_____

_____

_____

Name of Authorizing Official of Cooperating Institution _____

Title of Authorizing Official _____

Official Signature _____

Telephone Number _____

Whenever the nature of the project is such that the situation is deemed sensitive (as when anonymous donors in a cooperating institution provide fetal material or the investigator's interest in body fluids is in restricted drug metabolites), special precautions may be required whether or not the subjects are at risk.

G. Retention of Records

Copies of all documents presented or required for initial and continuing review by the Institutional Review Board, such as:

- IRB meeting minutes
- Documents presented for review
- Transmittals of IRB actions, instructions and conditions resulting from IRB deliberations
- Records of consent for subjects at risk

will be retained by the UIUC, subject to the terms and conditions of the grant or contract supporting the project, if any. As long as the Responsible Project Investigator remains at UIUC, he/she will store the records of subjects' consent. All other documents will be stored in the Office of the Executive Secretary of the Institutional Review Board. If the Responsible Project Investigator leaves the UIUC, the records of subjects' consent must either be turned over to the Executive Secretary of the Institutional Review Board or if the project will be continuing, to the succeeding Responsible Project Investigator. In the latter case, the IRB must be notified of the change in Responsible Project Investigator.

Usually a period of five years beyond the expiration of the project support in the case of an externally funded project, or five years beyond the termination of the project in a non-externally funded activity, will be sufficient for compliance with the institution's responsibilities.

However, cognizance should be taken of the implications of the Illinois statute of limitations and discovery. Legal counsel is deemed advisable. It should be noted that consent and other important records relating to the use of minors as subjects should be kept until at least two years after the minor reaches majority.

H. Institutional Review Board Responsibilities

1. Activities which require Institutional Review Board review collectively, but not individually.

The Institutional Review Board will review guidelines proposed by departments or units for activities which involve subjects at no risk beyond those of ordinary life and which are undertaken without external funding. The specific requirements for such departmental guidelines are set forth in Appendix B.

2. Activities involving human subjects which require Institutional Review Board review individually.

The Institutional Review Board will examine the material submitted by the investigator (Form IRB-1 and attachments). At its discretion the IRB may request additional information from the investigator to be submitted either orally or in writing and/or the IRB or its Advisory Committee may arrange to discuss the proposed activity with the investigator.

The Institutional Review Board will determine whether subjects will be placed at risk, and if risk is involved, whether

a) the risks to the subjects are so out weighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the project to be undertaken;

b) the rights and welfare of any such subjects will be adequately protected;

c) legally effective informed consent will be obtained by adequate and appropriate methods in accordance with applicable policy, laws and regulations.

At its discretion the Institutional Review Board may seek the advice of members of one or more of the Advisory Committees established for this purpose. These Advisory Committees are each composed of individuals selected for their familiarity with research in specified areas and also individuals who can provide the perspective of other disciplines. The Board may accept or reject the advice of the Advisory Committee members in taking its action on the proposal.

The Executive Secretary of the Institutional Review Board will inform the investigator, the department, and where required, appropriate office of DHEW or other sponsoring agencies, of the determination by the Institutional Review Board. When an application must be submitted to an

external agency prior to completion of the IRB review of the use of human subjects, the Executive Secretary may inform the agency that review is pending, indicating the date at which the IRB review is expected to be completed. The final disposition of the review will be promptly forwarded to the external agency, whatever the outcome.

All projects will receive at least an annual review. When the Institutional Review Board feels that the element of risk warrants an earlier review it may specify a specific review date or it may specify a stage of progress in the study at which a further review will be required. When the nature of the subjects or project is such that closer monitoring of the project is deemed advisable by the IRB or required by the funding agency, the IRB will specify the procedures to be followed in accomplishing the review. IRB approval of a project signifies that such matters have been considered and that the project is in compliance with applicable policies and regulations.

3. Adjudication of Differences and Review of Problems.

The Institutional Review Board will adjudicate matters involving human subjects in which the investigator and either the unit executive officer or Advisory Committee disagree.

The Institutional Review Board will review all problems involving human subjects and will be available to hear any complaints or concerns raised by subjects. On the basis of this review, the IRB will indicate the appropriate action to be taken, if any.

4. Documentation of Review.

The Executive Secretary of the Institutional Review Board will keep appropriate and informative records of the IRB's review of applications and activities, and other documentation as required by external sponsors and applicable laws and regulations.

5. Development of Information for Investigators, Reviewers, and Subjects.

The Secretary of the Institutional Review Board, working with IRB, will see that the information provided to departments, investigators, and reviewers is adequate and up to date, and will make sure that such information is accessible to subjects and prospective subjects.

Copies of this document, the UIUC General Assurance submitted to DHEW, and the various ethical codes referenced in Part I of this document will be on file in the Reference Department of the University Library and in the Office of the Executive Secretary of the Institutional Review Board. Copies of this document will be made available to the departments for distribution to investigators and also to subjects and prospective subjects upon their request.

6. Development of Policy and Procedures.

The Institutional Review Board also has responsibility for the development of new or revised policy and procedures to assure protection of human subjects, as necessary.

I. Investigator's Responsibilities

Each investigator is responsible for:

1. Being thoroughly familiar with

   a) the University's policy and the definitions of commonly used terms, as set forth in Part II of this document

   b) the Instructions for Investigators in Appendix E of this document

   c) applicable regulations of any external agencies providing support for the activity

   d) applicable policies of any cooperating institutions allowing access to subjects

2. Providing the information required and taking all the steps indicated in the appropriate procedure described in Part III, Section D of this document for initial and continuing review.

3. Maintaining records of informed consent for subjects at risk in compliance with applicable laws and regulations.

4. Protecting rights and welfare of the human subjects involved in his/her projects.

J. Unit Executive Officer's Responsibilities

The Unit Executive Officer has responsibility for:

1. Developing Departmental Guidelines, if appropriate, and submitting them to IRB for review.

2. Reviewing non-externally funded activities involving human subjects for compliance with approved departmental guidelines and forwarding to IRB for review any activities which are not within the approved departmental guidelines.

Providing further reviews of any such activity for which procedures involving human subjects are changed, and updating reviews of activities which continue longer than the approved period ($\leq$ 1 year).

3. Reviewing externally funded activities involving human subjects to assure that the Proposal Transmittal Form is correctly marked with regard to the use of human subjects.

4. Notifying the IRB of any problems which arise involving human subjects.

5. Assuring that faculty, staff, and students in the department are well-informed about the policies, procedures and ethical issues involved in the use of human subjects in experimentation.

K. Administrative Oversight

The administrative oversight of the Institutional Review Board's activities is the responsibility of the Vice Chancellor for Research, who appoints the members of the IRB. The Vice Chancellor keeps informed about the IRB matters through occasional attendance at IRB meetings and through the Executive Secretary of the IRB who is on the Vice Chancellor's staff. The Vice Chancellor reports on the IRB activities at each annual meeting of the Graduate Faculty.

L. Subject's Privileges

If a subject or prospective subject wishes to review the UIUC policies and procedures, he/she may request a copy from the department executive officer or the Executive Secretary of the Institutional Review Board, or may review it in the Reference Room of the University Library. Copies of the UIUC Assurance filed with DHEW are available in the Office of the Executive Secretary of the Institutional Review Board. One copy is on file in the University Library Reference Room.

If a subject wishes to voice complaints or concerns regarding his/her participation in a project, he/she should take the matter to the executive officer* of the department in which the activity is supervised. The subject may, if not satisfied with the results of that process, refer his/her concerns to the Executive Secretary of the Institutional Review Board, who will arrange for the matter to be considered by the Institutional Review Board.

M. University Provisions to Protect Health and Safety of Human Subjects

The university maintains McKinley Health Center, which includes a hospital having 58 beds, the usual hospital facilities, and a staff of physicians. This facility is available for emergencies that may arise in course of UIUC activities involving human subjects. Arrangements may

*Unit executive officers are responsible for notifying the Institutional Review Board of any problems which arise involving human subjects.

be made for physicians from McKinley Health Center or from local hospitals to monitor work involving human subjects when the Institutional Review Board finds the element of risk to warrant supervision by medical personnel.

INSTRUCTIONS FOR USE OF RESEARCH CONSENT FORMS

APPENDIX A

INSTRUCTIONS FOR USE OF RESEARCH CONSENT FORMS*

Adult Consent

1. If space is not adequate for an appropriate "Purpose" or "Nature of Experiment," place "See attached sheet" in the space and attach a sheet.

2. Repeat the procedures which are experimental, if they must also be set out in the "Nature of Experiment" to make the project understandable.

3. If there are no "Personal Risks," or "Appropriate Alternative Procedures," simply state that there are none.

4. Either paragraph A or B should apply. When retyping, eliminate the one which does not.

5. If further explanation beyond what is written on the form is required to be sure subject understands the risk, the witness should hear the explanation and sign the form.

6. The explanation should be made by the staff member, and the signature obtained by him personally.

7. Provide the telephone number of the individual who will be available to answer any future inquiries the subject may have.

8. Provide the subject with a copy of the consent form.

Minor's Consent

1. Your common sense and professional judgment should indicate when you should ask a minor to sign, and when you should ask simply for the signature of parents or guardians.

2. Use the minor's consent form for anyone under eighteen years of age.

3. Where a minor signs his consent, the parents or guardians must also sign.

Sample Consent Form for Obtaining Blood Samples for Research

1. Although subjects are not necessarily considered to be "at risk" when project involves venipuncture, the Institutional Review Board has agreed to require obtaining written informed consent for these projects.

2. The language of the Sample Form provides an explanation of the procedure which should be comprehensible to most subjects.

*For further discussion and instructions about the requirements for obtaining legally effective informed consnet, see Part II pages 5 and 6, Appendix D, sections 46.9 and 46.10, and Appendix E pages 3 through 5.

CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

I, _____, state that I am over eighteen
(Name of Volunteer)

(18) years of age and wish to participate in a program of research being conducted by _____.
(Name of Staff Member)

The purpose of the research is:_____

_____

_____.

The project involves_____
(Nature of Experiment)

_____

_____.

The experimental procedures are _____

_____.

The personal risks involved are: _____

_____

_____.

Appropriate alternative procedures which might benefit me personally are:_____

_____

_____.

(Strike our A or B)

A) I acknowledge that I have been informed that this procedure is not intended to benefit my personal health.

B) I acknowledge that I have been informed that this procedure is also designed to assist in maintaining or improving my personal health and will benefit me personally in the following way_____

_____

_____.

I acknowledge that _____ has fully
(Name of Staff Member)
explained to me the risks involved and the need for the research; has informed me that I may withdraw from participation at anytime; has offered to answer any inquiries which I may make concerning the procedures to be followed; and has informed me that I will be given a copy of this consent form. I freely and voluntarily consent to my participation in this research project.

_____
(Signature of Volunteer)

_____
(Signature of Staff Member)

_____
Witness to explanation
(not to signature)

_____
Date

MINOR'S CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

I, _____, state that I am _____
(Name of Volunteer)
years of age and wish to participate in a program of research being conducted by _____.
(Name of Staff Member)

The purpose of the research is: _____

_____

_____.

The project involves _____
(Nature of Experiment)

_____

_____.

The experimental procedures are _____

_____.

The personal risks involved are: _____

_____

_____.

Appropriate alternative procedures which might benefit me personally are: _____

_____

_____.

I acknowledge that _____ has fully
(Name of Staff Member)
explained to me the risks involved and the need for the research; has informed me that I may withdraw from participation at anytime; has offered to answer any inquiries which I may make concerning the procedures to be followed; and has informed me that I will be given a copy of this consent form. I freely and voluntarily consent to my participation in this research project.

_____
(Signature of Volunteer)

PARENTAL CONSENT

We, parents or guardians of the above minor volunteer, agree to the participation of the above minor in the research project set out above. We have been informed of the need for the research, the benefits to be derived from it, and the risks involved and that we may withdraw him/her from participation at any time. We have also been informed that the research can best be conducted with a subject population including minors because of the nature of the research.

(Strike out A or B).

A) Being aware of the value of the participation of minors in this research project and further being aware that this procedure will not benefit the minor here involved personally, we consent to the minor's participation.

B) Being aware of the value of the participation of minors in this research project and being informed that the procedures will also benefit the above-named minor personally in the following way _____

_____

_____

_____

_____

we consent to the minor's participation.

_____ _____

Signature of Staff Member Signature of Parents or Guardians

_____ _____

Witness to explanation (not to signature) Signature of Parents or Guardians

_____

Date

CONSENT FOR BLOOD TO BE DRAWN FOR USE IN A RESEARCH PROJECT

I, _____, state that I am over eighteen (18)
(Name of Human Subject)

years of age and wish to participate in a program of research being conducted by _____.
(Name of Responsible Project Investigator)

Brief Description of the Project: (Include purpose.)

The experimental procedure for the human subject is to donate _____
(number)

samples of _____ of blood at intervals of
(# of cc's, # of ounces)

_____.
(indicate frequency)

The blood will be drawn by a certified medical technologist, nurse, or other suitably qualified person.

The personal risks involved are: Slight pain during the drawing of blood and in rare cases development of what is commonly known as "black and blue mark" caused by minor seeping of blood around the puncture.

I acknowledge that I have been informed that this procedure is not intended to benefit my personal health.

I acknowledge that _____ has fully explained
(Responsible Project Investigator)
to me the risks involved and the need for the research, has informed me that I may withdraw from participation at anytime and has offered to answer any inquiries which I may make concerning the procedures to be followed. I freely and voluntarily consent to my participation in this research project.

_____
(Signature of Human Subject)

_____
(Signature of Responsible Project Investigator)

_____
(Telephone number of Responsible Project Investigator)

_____
(Date)

DEVELOPMENT OF DEPARTMENTAL GUIDELINES FOR THE REVIEW OF ACTIVITIES INVOLVING HUMAN SUBJECTS

Appendix B

DEVELOPMENT OF DEPARTMENTAL GUIDELINES FOR THE REVIEW OF ACTIVITIES INVOLVING HUMAN SUBJECTS.

A large number of activities involving human subjects at no risk beyond those of ordinary life are undertaken each year without external funding. Some are, for example, part of introductory and research methods courses; some are short term pilot projects, doctoral dissertations and independent study projects. Some are regular faculty research projects. Some involve new use of previously gathered data on human subjects.

The large volume of such activities, the fact that for most of these any risks to the human subjects falls well within the risks of ordinary life, and the fact that for many the time available for review is extremely short, dictate that review must be expeditious and simple as well as responsible.

Review of such activities may be handled by the establishment of departmental guidelines on the basis of the recurring types of "ordinary risk" activities undertaken by the department and the well established and accepted professional procedures used in the department. When such departmental guidelines have been approved by the Institutional Review Board, activities involving human subjects, which are not externally funded, and which fall within the departmental guidelines, would not need to be reviewed individually by the IRB.

Departments wishing to use this review mechanism must submit written guidelines to the IRB which will review them to be sure that the IRB's responsibilities can be fulfilled.

To be approved by the IRB Departmental Guidelines must:

a) identify the types of activities involving human subjects which are normally undertaken by the department and with which the department has had sufficient experience to be able to set standards for appropriate conduct.

b) define the standards with which such activities would have to comply.

c) assure that the activities fall in Category 1, i.e., involve no risks exceeding those of ordinary life. (See Part II, Pages 6-10) Note that activities which involve administration of any drugs or noxious stimuli, and/or situations which might involve psychological stress are considered to fall outside the departmental guidelines and therefore require IRB review.

d) assure that the participation of human subjects is voluntary.

e) assure careful attention to the adequacy of protection of the rights, and welfare of human subjects for the "ordinary" risks that are imposed.

f) assure the privacy of individuals and small identifiable groups, by appropriate procedures and commitments for confidentiality of data.

g) assure consideration of the potential benefit/risk ratio.

h) describe the department's plan for assuring that all projects involving human subjects which are not sent forward for IRB review, meet the departmental standards. (Some departments may establish internal review committees, or assign review responsibility to an individual. Some departments may rely on careful and continuing instruction and more informal communication routes.)

i) provide for sufficient documentation so that reports can be made to the IRB on the department's experience with this decentralized review process.

Note: 1. All externally funded projects or activities involving human subjects must be reviewed by the Institutional Review Board.

2. Any project or activity involving subjects at risk beyond those of ordinary life must be submitted for review by the Institutional Review Board.

3. Any project or activity involving human subjects which does not fall within the departmental guidelines must be reviewed by the Institutional Review Board.

4. The Institutional Review Board is available to review any project or activity upon request. In carrying out its oversight responsibility the Institutional Review Board may review any UIUC project or activity involving human subjects, whether or not it falls within departmental guidelines.

5. Until departmental guidelines have been developed and approved by the Institutional Review Board, all projects/activities involving human subjects must be reviewed by the Institutional Review Board.

FORM IRB-1
INFORMATION FOR REVIEW OF ACTIVITY INVOLVING HUMAN SUBJECTS

Information for Review of Activity involving Human Subjects

(If submitted to IRB for review, submit 11 copies of this form and 1 copy of proposal for project to be undertaken.)

Name of Responsible Project Investigator	2. Name of Investigator, if different

Title of Project - Purpose

Funding Agency to which submitted, if any,	5. Grant or Contract Number, if any,	6. Project Perio

Type of Project

- ☐ Research
- ☐ Demonstration
- ☐ Class Project
- ☐ Independent Study
- ☐ Other

8. Type of Investigator

- ☐ Faculty
- ☐ Staff
- ☐ Graduate Student
- ☐ Undergrad. Student

9. Type of Subject

A.
- ☐ Adult, non-student
- ☐ UIUC student
- ☐ Minor
- ☐ Other (explain)

B.
- ☐ Normal volunteer
- ☐ In-patient
- ☐ Out-patient
- ☐ Individual with limite civil freedom
- ☐ Mentally retarded or disabled
- ☐ Pregnant women, fetuse newborn, dead

Number of Subjects to be involved _____

Number of Controls to be involved _____

- ☐ Project involves use of drugs not certified by FDA for clinical use for this purpose.
- ☐ Subjects will receive payment or some form of compensation for participation.
- ☐ Access to subjects will be gained through cooperating institutions.
- ☐ Written consent form will be obtained. (Attach copy of form to be used.)

NOTE: All investigators using human subjects should be thoroughly familiar with the definitions, instructions, policies and procedures described in The Use of Human Subjects in Research at the University of Illinois - Urbana-Champaign. (Available from the Executive Secretary, Institutional Review Board, Graduate College.)

Describe the methods to be used for obtaining subjects for this work and for assuring that their participation is voluntary.

Describe how subjects will be used.

(OVER)

14. Will the subjects in the proposed work be placed "at risk" as defined in The Use of Human Subjects in Research at the University of Illinois - Urbana-Champaign?

☐ Yes ☐ No ☐ Uncertain

15. If the response to item 14 is "No", briefly indicate your reasons for this response.

16. If the response to item 14 is "Yes" or "Uncertain", provide the following information: (Use additional pages)

a. Describe the possible risks to the subject and the potential benefits to the subject and/or to others.

b. Describe the method to be used for securing legally effective informed consent of subjects. Attach copy of the consent form and any oral or written explanation to be used.

c. Describe the provisions for safeguarding the rights and welfare of the human subje to be involved in this work, including the provisions for assuring confidentiality of data and any provisions for medical care or supervision.

Certifications:

1. I am familiar with The Use of Human Subjects in Research at the University of Illinois Urbana-Champaign. I subscribe to the standards described therein and will adhere to the policies and procedures explained therein.

2. Should changes in procedures involving human subjects become advisable, I will submit them for review prior to initiating the change.

3. If any problems involving human subjects emerge, I will immediately notify the unit executive officer and the Executive Secretary of the Institutional Review Board.

Date_____ Signatures:_____ _____

Responsible Project Investigator (RPI) Department

_____

Investigator, if different from RPI

For optional departmental use:

The activity described herein is in conformity with IRB approved departmental guideli

_____ _____

Unit executive officer (or his designee) Date

DHEW REGULATIONS

federal register

THURSDAY, MARCH 13, 1975

WASHINGTON, D.C.

Volume 40 ■ Number 50

PART II

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Office of the Secretary

■

PROTECTION OF HUMAN SUBJECTS

Technical Amendments

Title 45—Public Welfare

SUBTITLE A—DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE, GENERAL ADMINISTRATION

PART 46—PROTECTION OF HUMAN SUBJECTS

Technical Amendments

On May 30, 1974, final regulations were published in the FEDERAL REGISTER (39 FR 18914) relating to protection of human subjects in research, development, and related activities supported by Department of Health, Education, and Welfare grants and contracts. Shortly thereafter, on July 12, 1974, the National Research Act, Public Law 93-348, was enacted. Although the Conference Report on the bill (H.R. 7724) which later became Pub. L. 93-348 expressed satisfaction with the regulations (H. Rep. No. 93-1148, at p. 26), section 212(a) of said Law added a new section 474(a) to the Public Health Service Act, which provides as follows:

> The Secretary shall by regulation require that each entity which applies for a grant or contract under this Act for any project or program which involves the conduct of biomedical or behavioral research involving human subjects submit in or with its application for such grant or contract assurances satisfactory to the Secretary that it has established (in accordance with regulations which the Secretary shall prescribe) a board (to be known as an 'Institutional Review Board') to review biomedical and behavioral research involving human subjects conducted at or sponsored by such entity in order to protect the rights of human subjects of such research.

Section 212(b) of Pub. L. 93-348 further stated that the regulations required to carry out section 474(a) shall apply with respect to applications for grants and contracts under the Public Health Service Act submitted after promulgation of such regulations.

The regulations published on May 30, 1974, codified at 45 CFR Part 46, would with minor, technical changes fully implement section 474(a). This would be accomplished by: (1) amending the citation of AUTHORITY to refer to section 474(a), (2) substituting references to "institutions" and "Institutional Review Boards" for existing references to "organizations" and "committees" and making related changes, and (3) revising 45 CFR 46.7, 46.11(a), and 46.12 to take account of the requirement in section 474 (a) that an assurance concerning establishment of a Board must in all cases be submitted in or with the application. Since Part 46 was published initially as a notice of proposed rulemaking (38 FR 27882), and since the aforesaid changes would be minor and technical in nature, it is unnecessary to publish such changes as a notice of proposed rulemaking. The Department therefore finds that good cause exists for dispensing with this step.

Accordingly, the regulations published in the FEDERAL REGISTER on May 30, 1974 and codified at 45 CFR Part 46, as so amended, are hereby adopted as final regulations implementing section 474(a) of the Public Health Service Act, effective March 13, 1975.

Dated: February 14, 1975.

THEODORE COOPER,
Acting Assistant Secretary for Health.

Approved: March 7, 1975.

CASPAR W. WEINBERGER,
Secretary.

Therefore, Subtitle A of Title 45 of the Code of Federal Regulations is amended by revising Part 46 to read as follows:

Sec.

AUTHORITY: 5 U.S.C. 301; sec. 474(a), 88 Stat. 352 (42 U.S.C. 2891-3(a)).

§ 46.1 Applicability.

(a) The regulations in this part are applicable to all Department of Health, Education, and Welfare grants and contracts supporting research, development, and related activities in which human subjects are involved.

(b) The Secretary may, from time to time, determine in advance whether specific programs, methods, or procedures to which this part is applicable place subjects at risk, as defined in § 46.3(b). Such determinations will be published as notices in the FEDERAL REGISTER and will be included in an appendix to this part.

§ 46.2 Policy.

(a) Safeguarding the rights and welfare of subjects at risk in activities supported under grants and contracts from DHEW is primarily the responsibility of the institution which receives or is accountable to DHEW for the funds awarded for the support of the activity. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of DHEW that no activity involving human subjects to be supported by DHEW grants or contracts shall be undertaken unless an Institutional Review Board has reviewed and approved such activity, and the institution has submitted to DHEW a certification of such review and approval, in accordance with the requirements of this part.

(b) This review shall determine whether these subjects will be placed at risk, and, if risk is involved, whether:

(1) The risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept these risks;

(2) the rights and welfare of any such subjects will be adequately protected;

(3) legally effective informed consent will be obtained by adequate and appropriate methods in accordance with the provisions of this part; and

(4) the conduct of the activity will be reviewed at timely intervals.

(c) No grant or contract involving human subjects at risk shall be made to an individual unless he is affiliated with or sponsored by an institution which can and does assume responsibility for the subjects involved.

§ 46.3 Definitions.

(a) "Institution" means any public or private institution or agency (including Federal, State, and local government agencies).

(b) "Subject at risk" means any individual who may be exposed to the possibility of injury, including physical, psychological, or social injury, as a consequence of participation as a subject in any research, development, or related activity which departs from the application of those established and accepted methods necessary to meet his needs, or which increases the ordinary risks of daily life, including the recognized risks inherent in a chosen occupation or field of service.

(c) "Informed consent" means the knowing consent of an individual or his legally authorized representative, so situated as to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress, or other form of constraint or coercion. The basic elements of information necessary to such consent include:

(1) A fair explanation of the procedures to be followed, and their purposes, including identification of any procedures which are experimental;

(2) a description of any attendant discomforts and risks reasonably to be expected;

(3) a description of any benefits reasonably to be expected;

(4) a disclosure of any appropriate alternative procedures that might be advantageous for the subject;

(5) an offer to answer any inquiries concerning the procedures; and

(6) an instruction that the person is free to withdraw his consent and to discontinue participation in the project or activity at any time without prejudice to the subject.

(d) "Secretary" means the Secretary of Health, Education, and Welfare or any other officer or employee of the Department of Health, Education, and Welfare to whom authority has been delegated.

(e) "DHEW" means the Department of Health, Education, and Welfare.

(f) "Approved assurance" means a document that fulfills the requirements of this part and is approved by the Secretary.

(g) "Certification" means the official institutional notification to DHEW in accordance with the requirements of this part that a project or activity involving human subjects at risk has been reviewed and approved by the institution in accordance with the "approved assurance" on file at DHEW.

(h) "Legally authorized representative" means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to such subject's participation in the particular activity or procedure.

§ 46.4 Submission of assurances.

(a) Recipients or prospective recipients of DHEW support under a grant or contract involving subjects at risk shall provide written assurance acceptable to DHEW that they will comply with DHEW policy as set forth in this part. Each assurance shall embody a statement of compliance with DHEW requirements for initial and continuing Institutional Review Board review of the supported activities; a set of implementing guidelines, including identification of the Board and a description of its review procedures; or, in the case of special assurances concerned with single activities or projects, a report of initial findings of the Board and of its proposed continuing review procedures.

(b) Such assurance shall be executed by an individual authorized to act for the institution and to assume on behalf of the institution the obligations imposed by this part, and shall be filed in such form and manner as the Secretary may require.

§ 46.5 Types of assurances.

(a) *General assurances.* A general assurance describes the review and implementation procedures applicable to all DHEW-supported activities conducted by an institution regardless of the number, location, or types of its components or field activities. General assurances will be required from institutions having a significant number of concurrent DHEW-supported projects or activities involving human subjects.

(b) *Special assurances.* A special assurance will, as a rule, describe those review and implementation procedures applicable to a single activity or project. A special assurance will not be solicited or accepted from an institution which has on file with DHEW an approved general assurance.

§ 46.6 Minimum requirements for general assurances.

General assurances shall be submitted in such form and manner as the Secretary may require. The institution must include, as part of its general assurance, implementing guidelines that specifically provide for:

(a) A statement of principles which will govern the institution in the discharge of its responsibilities for protecting the rights and welfare of subjects. This may include appropriate existing codes or declarations, or statements formulated by the institution itself. It is to be understood that no such principles supersede DHEW policy or applicable law.

(b) An Institutional Review Board or Board structure which will conduct initial and continuing reviews in accordance with the policy outlined in § 46.2. Such Board structure or Board shall meet the following requirements:

(1) The Board must be composed of not less than five persons with varying backgrounds to assure complete and adequate review of activities commonly conducted by the institution. The Board must be sufficiently qualified through the maturity, experience, and expertise of its members and diversity of its membership to insure respect for its advice and counsel for safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific activities, the Board must be able to ascertain the acceptability of applications and proposals in terms of institutional commitments and regulations, applicable law, standards of professional conduct and practice, and community attitudes. The Board must therefore include persons whose concerns are in these areas.

(2) The Board members shall be identified to DHEW by name; earned degrees, if any; position or occupation; representative capacity; and by other pertinent indications of experience such as board certification, licenses, etc., sufficient to describe each member's chief anticipated contributions to Board deliberations. Any employment or other relationship between each member and the institution shall be identified, i.e., full-time employee, part-time employee, member of governing panel or board, paid consultant, unpaid consultant. Changes in Board membership shall be reported to DHEW in such form and at such times as the Secretary may require.

(3) No member of a Board shall be involved in either the initial or continuing review of an activity in which he has a conflicting interest, except to provide information requested by the Board.

(4) No Board shall consist entirely of persons who are officers, employees, or agents, of, or are otherwise associated with the institution, apart from their membership on the Board.

(5) No Board shall consist entirely of members of a single professional group.

(6) The quorum of the Board shall be defined, but may in no event be less than a majority of the total membership duly convened to carry out the Board's responsibilities under the terms of the assurance.

(c) Procedures which the institution will follow in its initial and continuing review of applications, proposals, and activities.

(d) Procedures which the Board will follow (1) to provide advice and counsel to activity directors and investigators with regard to the Board's actions. (2) to insure prompt reporting to the Board of proposed changes in an activity and of unanticipated problems involving risk to subjects or others, and (3) to insure that any such problems, including adverse reactions to biologicals, drugs, radioisotope labelled drugs, or to medical devices, are promptly reported to DHEW.

(e) Procedures which the institution will follow to maintain an active and effective Board and to implement its recommendations.

§ 46.7 Minimum requirements for special assurances.

Special assurances shall be submitted in such form and manner as the Secretary may require. An acceptable special assurance shall:

(a) Identify the specific grant or contract involved by its full title; and by the name of the activity or project director, principal investigator, fellow, or other person immediately responsible for the conduct of the activity.

(b) Include a statement, executed by an appropriate institutional official, indicating that the institution has established an Institutional Review Board satisfying the requirements of § 46.6(b).

(c) Describe the makeup of the Board and the training, experience, and background of its members, as required by § 46.6(b)(2).

(d) Describe in general terms the risks to subjects that the Board recognizes as inherent in the activity, and justify its decision that these risks are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant the Board's decision to permit the subject to accept these risks.

(e) Describe the informed consent procedures to be used and attach documentation as required by § 46.10.

(f) Describe procedures which the Board will follow to insure prompt reporting to the Board of proposed changes in the activity and of any unanticipated problems, involving risks to subjects or others and to insure that any such problems, including adverse reactions to biologicals, drugs, radioisotope labelled drugs, or to medical devices are promptly reported to DHEW.

(g) Indicate at what time intervals the Board will meet to provide for continuing review. Such review must occur no less than annually.

(h) Be signed by the individual members of the Board and be endorsed by an appropriate institutional official.

§ 46.8 Evaluation and disposition of assurances.

(a) All assurances submitted in accordance with §§ 46.6 and 46.7 shall be

evaluated by the Secretary through such officers and employees of DHEW and such experts or consultants engaged for this purpose as he determines to be appropriate. The Secretary's evaluation shall take into consideration, among other pertinent factors, the adequacy of the proposed Institutional Review Board in the light of the anticipated scope of the applicant institution's activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in the light of the probable risks, and the size and complexity of the institution.

(b) On the basis of his evaluation of an assurance pursuant to paragraph (a) of this section, the Secretary shall (1) approve, (2) enter into negotiations to develop a more satisfactory assurance, or (3) disapprove. With respect to approved assurances, the Secretary may determine the period during which any particular assurance or class of assurances shall remain effective or otherwise condition or restrict his approval. With respect to negotiations, the Secretary may, pending completion of negotiations for a general assurance, require an institution otherwise eligible for such an assurance, to submit special assurances.

§ 46.9 Obligation to obtain informed consent; prohibition of exculpatory clauses.

Any institution proposing to place any subject at risk is obligated to obtain and document legally effective informed consent. No such informed consent, oral or written, obtained under an assurance provided pursuant to this part shall include any exculpatory language through which the subject is made to waive, or to appear to waive, any of his legal rights, including any release of the institution or its agents from liability for negligence.

§ 46.10 Documentation of informed consent.

The actual procedure utilized in obtaining legally effective informed consent and the basis for Institutional Review Board determinations that the procedures are adequate and appropriate shall be fully documented. The documentation of consent will employ one of the following three forms:

(a) Provision of a written consent document embodying all of the basic elements of informed consent. This may be read to the subject or to his legally authorized representative, but in any event he or his legally authorized representative must be given adequate opportunity to read it. This document is to be signed by the subject or his legally authorized representative. Sample copies of the consent form as approved by the Board are to be retained in its records.

(b) Provision of a "short form" written consent document indicating that the basic elements of informed consent have been presented orally to the subject or his legally authorized representative. Written summaries of what is to be said to the patient are to be approved by the Board. The short form is to be signed by the subject or his legally authorized representative and by an auditor witness to the oral presentation and to the subject's signature. A copy of the approved summary, annotated to show any additions, is to be signed by the persons officially obtaining the consent and by the auditor witness. Sample copies of the consent form and of the summaries as approved by the Board are to be retained in its records.

(c) Modification of either of the primary procedures outlined in paragraphs (a) and (b) of this section. Granting of permission to use modified procedures imposes additional responsibility upon the Board and the institution to establish: (1) that the risk to any subject is minimal, (2) that use of either of the primary procedures for obtaining informed consent would surely invalidate objectives of considerable immediate importance, and (3) that any reasonable alternative means for attaining these objectives would be less advantageous to the subjects. The Board's reasons for permitting the use of modified procedures must be individually and specifically documented in the minutes and in reports of Board actions to the files of the institution. All such modifications should be regularly reconsidered as a function of continuing review and as required for annual review, with documentation of reaffirmation, revision, or discontinuation, as appropriate.

§ 46.11 Submission and certification of applications and proposals, general assurances.

(a) *Timely review.* Any institution having an approved general assurance shall indicate in each application or proposal for support of activities covered by this part (or in a separate document submitted with such application or proposal) that it has on file with DHEW such an assurance. In addition, unless the Secretary otherwise provides, each such application or proposal must be given review and, when found to involve subjects at risk, approval, prior to submission to DHEW. In the event the Secretary provides for the performance of institutional review of an application or proposal after its submission to DHEW, processing of such application or proposal by DHEW will under no circumstances be completed until such institutional review and approval has been certified. Except where the institution determines that human subjects are not involved, the application or proposal should be appropriately certified in the spaces provided on forms, or one of the following certifications, as appropriate, should be typed on the lower or right hand margin of the page bearing the name of an official authorized to sign or execute applications or proposals for the institution.

Human Subjects: Reviewed, Not at Risk.

(Date)

Human Subjects: Reviewed, At Risk, Approved

(Date)

(b) *Applications and proposals not certified.* Applications and proposals not properly certified, or submitted as not involving human subjects and found by the operating agency to involve human subjects, will be returned to the institution concerned.

§ 46.12 Submission and certification of applications and proposals, special assurances.

(a) Except as provided in paragraph (b) of this section, institutions not having an approved general assurance shall submit in or with each application or proposal for support of activities covered by this part a separate special assurance and certification of its review and approval.

(b) If the Secretary so provides, the assurance which must be submitted in or with the application or proposal under paragraph (a) of this section need satisfy only the requirements of § 46.7(a) and § 46.7(b) of this part. Under such circumstances, processing of such application or proposal by DHEW will not be completed until a further assurance satisfying the remaining requirements of § 46.7 has been submitted to DHEW

(c) An assurance and certification prepared in accordance with this part and approved by DHEW shall be considered to have met the requirement for certification for the initial grant or contract period concerned. If the terms of the grant or contract recommend additional support periods, each application or proposal for continuation or renewal of support must satisfy the requirements of this section or § 46.11 whichever is applicable at the time of its submission.

§ 46.13 Applications and proposals lacking definite plans for involvement of human subjects.

Certain types of applications or proposals are submitted with the knowledge that subjects are to be involved within the support period, but definite plans for this involvement would not normally be set forth in the application or proposal. These include such activities as (a) institutional type grants where selection of projects is the responsibility of the institution, (b) training grants where training projects remain to be selected, and (c) research, pilot, or developmental studies in which involvement depends upon such things as the completion of instruments, or of prior animal studies, or upon the purification of compounds. Such applications or proposals shall be reviewed and certified in the same manner as more definitive applications or proposals. The initial certification indicates institutional approval of the applications or proposals as submitted, and commits the institution to later review of the plans when completed. Such later review and certification to DHEW should be completed prior to the beginning of the budget period during which actual involvement of human subjects is to begin. Review and certification to DHEW must in any event be completed prior to involvement of human subjects.

§ 46.14 Applications and proposals submitted with the intent of not involving human subjects.

If an application or proposal does not anticipate involving or intend to involve human subjects, no certification should be included with the initial submission of the application or proposal. In those instances, however, when later it becomes appropriate to use all or part of awarded funds for one or more activities which will involve subjects, each such activity shall be reviewed and approved in accordance with the assurance of the institution prior to the involvement of subjects. In addition, no such activity shall be undertaken until the institution has submitted to DHEW: (a) a certification that the activity has been reviewed and approved in accordance with this part, and (b) a detailed description of the proposed activity (including any protocol or similar document). Also, where support is provided by project grants or contracts, subjects shall not be involved prior to certification and institutional receipt of DHEW approval and, in the case of contracts, prior to negotiation and approval of an amended contract description of work.

§ 46.15 Evaluation and disposition of applications and proposals.

(a) Notwithstanding any prior review, approval, and certification by the institution all applications or proposals involving human subjects at risk submitted to DHEW shall be evaluated by the Secretary for compliance with this part through such officers and employees of the Department and such experts or consultants engaged for this purpose as he determines to be appropriate. This evaluation may take into account, among other pertinent factors, the apparent risks to the subjects, the adequacy of protection against these risks, the potential benefits of the activity to the subjects and to others, and the importance of the knowledge to be gained.

(b) Disposition. On the basis of his evaluation of an application or proposal pursuant to paragraph (a) of this section and subject to such approval or recommendation by or consultation with appropriate councils, committees, or other bodies as may be required by law, the Secretary shall (1) approve, (2) defer for further evaluation, or (3) disapprove support of the proposed activity in whole or in part. With respect to any approved grant or contract, the Secretary may impose conditions, including restrictions on the use of certain procedures, or certain subject groups, or requiring use of specified safeguards or informed consent procedures when in his judgment such conditions are necessary for the protection of human subjects.

§ 46.16 Cooperative activities.

Cooperative activities are those which involve institutions in addition to the grantee or prime contractor (such as a contractor under a grantee or a subcontractor under a prime contractor). If, in such instances, the grantee or prime contractor obtains access to all or some of the subjects involved through one or more cooperating institutions, the basic DHEW policy applies and the grantee or prime contractor remains responsible for safeguarding the rights and welfare of the subjects.

(a) *Institution with approved general assurance.* Initial and continuing review by the institution may be carried out by one or a combination of procedures:

(1) Cooperating institution with approved general assurance. When the cooperating institution has on file with DHEW an approved general assurance, the grantee or contractor may, in addition to its own review, request the cooperating institution to conduct an independent review and to report its recommendations on those aspects of the activity that concern individuals for whom the cooperating institution has responsibility under its own assurance to the grantee's or contractor's Institutional Review Board. The grantee or contractor may, at its discretion, concur with or further restrict the recommendations of the cooperating institution. It is the responsibility of the grantee or contractor to maintain communication with the Boards of the cooperating institution. However, the cooperating institution shall promptly notify the grantee or contracting institution whenever the cooperating institution finds the conduct of the project or activity within its purview unsatisfactory.

(2) Cooperating institution with no approved general assurance. When the cooperating institution does not have an approved general assurance on file with DHEW, the DHEW may require the submission of a general or special assurance which, if approved, will permit the grantee or contractor to follow the procedure outlined in the preceding subparagraph.

(3) Interinstitutional joint review. The grantee or contracting institution may wish to develop an agreement with cooperating institutions to provide for an Institutional Review Board with representatives from cooperating institutions. Representatives of cooperating institutions may be appointed as ad hoc members of the grantee or contracting institution's existing Institutional Review Board or, if cooperation is on a frequent or continuing basis as between a medical school and a group of affiliated hospitals, appointments for extended periods may be made. All such cooperative arrangements must be approved by DHEW as part of a general assurance, or as an amendment to a general assurance.

(b) *Institutions with special assurances.* While responsibility for initial and continuing review necessarily lies with the grantee or contracting institution, DHEW may also require approved assurances from those cooperating institutions having immediate responsibility for subjects.

If the cooperating institution has on file with DHEW an approved general assurance, the grantee or contractor shall request the cooperating institution to conduct its own independent review of those aspects of the project or activity which will involve human subjects for which it has responsibility. Such a request shall be in writing and should provide for direct notification of the grantee's or contractor's Institutional Review Board in the event that the cooperating institution's Board finds the conduct of the activity to be unsatisfactory. If the cooperating institution does not have an approved general assurance on file with DHEW, it must submit to DHEW a general or special assurance which is determined by DHEW to comply with the provisions of this part.

§ 46.17 Investigational new drug 30-day delay requirement.

Where an institution is required to prepare or to submit a certification under §§ 46.11, 46.12, 46.13, or 46.14 and the application or proposal involves an investigational new drug within the meaning of The Food, Drug, and Cosmetic Act, the drug shall be identified in the certification together with a statement that the 30-day delay required by 21 CFR 312.1(a)(2) has elapsed and the Food and Drug Administration has not, prior to expiration of such 30-day interval, requested that the sponsor continue to withhold or to restrict use of the drug in human subjects; or that the Food and Drug Administration has waived the 30-day delay requirement; provided, however, that in those cases in which the 30-day delay interval has neither expired nor been waived, a statement shall be forwarded to DHEW upon such expiration or upon receipt of a waiver. No certification shall be considered acceptable until such statement has been received.

§ 46.18 Institution's executive responsibility.

Specific executive functions to be conducted by the institution include policy development and promulgation and continuing indoctrination of personnel. Appropriate administrative assistance and support shall be provided for the Board's functions. Implementation of the Board's recommendations through appropriate administrative action and followup is a condition of DHEW approval of an assurance. Board approvals, favorable actions, and recommendations are subject to review and to disapproval or further restriction by the institution officials. Board disapprovals, restrictions, or conditions cannot be rescinded or removed except by action of a Board described in the assurance approved by DHEW.

§ 46.19 Institution's records; confidentiality.

(a) Copies of all documents presented or required for initial and continuing review by the Institutional Review Board, such as Board minutes, records of subject's consent, transmittals on actions, instructions, and conditions resulting from Board deliberations addressed to the activity director, are to be retained by the institution, subject to the terms and conditions of grant and contract awards.

(b) Except as otherwise provided by law information in the records or possession of an institution acquired in con-

nection with an activity covered by this part, which information refers to or can be identified with a particular subject, may not be disclosed except:

(1) with the consent of the subject or his legally authorized representative; or

(2) as may be necessary for the Secretary to carry out his responsibilities under this part.

§ 46.20 Reports.

Each institution with an approved assurance shall provide the Secretary with such reports and other information as the Secretary may from time to time prescribe.

§ 46.21 Early termination of awards; evaluation of subsequent applications and proposals.

(a) If, in the judgment of the Secretary an institution has failed materially to comply with the terms of this policy with respect to a particular DHEW grant or contract, he may require that said grant or contract be terminated or suspended in the manner prescribed in applicable grant or procurement regulations.

(b) In evaluating applications or proposals for support of activities covered by this part, the Secretary may take into account, in addition to all other eligibility requirements and program criteria, such factors as: (1) whether the applicant or offeror has been subject to a termination or suspension under paragraph (a) of this section, (2) whether the applicant or offeror or the person who would direct the scientific and technical aspects of an activity has in the judgment of the Secretary failed materially to discharge his, her, or its responsibility for the protection of the rights and welfare of subjects in his, her, or its care (whether or not DHEW funds were involved), and (3) whether, where past deficiencies have existed in discharging such responsibility, adequate steps have in the judgment of the Secretary been taken to eliminate these deficiencies.

§ 46.22 Conditions.

The Secretary may with respect to any grant or contract or any class of grants or contracts impose additional conditions prior to or at the time of any award when in his judgment such conditions are necessary for the protection of human subjects.

[FR Doc.75-6621 Filed 3-12-75;8:45 am]

federal register

FRIDAY, AUGUST 8, 1975

PART III:

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Office of the Secretary

■

PROTECTION OF HUMAN SUBJECTS

Fetuses, Pregnant Women, and In Vitro Fertilization

Title 45—Public Welfare

SUBTITLE A—DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PART 46—PROTECTION OF HUMAN SUBJECTS

Fetuses, Pregnant Women, In Vitro Fertilization

Basic regulations governing the protection of human subjects involved in research development, and related activities supported or conducted by the Department through grants and contracts were published in the FEDERAL REGISTER on May 30, 1974 (39 FR 18914).[1] At that time it was indicated that notices of proposed rulemaking would be developed to provide additional protection for subjects of research who may have diminished capacity to provide informed consent. On August 23, 1974, a notice of proposed rulemaking was published for public comment (39 FR 30648) in which it was proposed to amend 45 CFR Part 46 to provide further protective measures for the fetus, the abortus, prisoners, and the institutionalized mentally disabled as subjects of research activities.

On July 12, 1974, the National Research Act (Pub. L. 93-348) was signed into law, thereby creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the charges to the Commission was to investigate and study the nature and extent of research involving the living human fetus and to recommend to the Secretary the circumstances (if any) under which such research should be conducted or supported by the Department. Pursuant to section 202(b) of that Act, the Commission has transmitted Recommendations to the Secretary. Pursuant to section 205 of the Act, the Secretary is publishing that Report elsewhere in this issue of the FEDERAL REGISTER.

After considering both the pubic comments to the proposed rulemaking published August 23, 1974, and the Recommendations of the Commission, the Secretary has determined to amend 45 CFR 46 by adding a subpart governing research involving the fetus, the pregnant woman, and products of human *in vitro* fertilization consistent with the public comments and the Recommendations of the Commission. This amendment to the regulations is to be effective immediately. The Secretary, as required by Pub. L. 93-348, section 205, will take into consideration any comments submitted regarding the Recommendations and, if it appears necessary, will propose further rulemaking with respect to any amendments to these regulations which appear warranted.

The Secretary also concludes that the moratorium on fetal research which was imposed by the Department on August 27, 1974 (39 FR 30962) may now be lifted, allowing research to go forward under the regulations issued herewith. The Secretary notes in this regard that the restrictions imposed by section 213 of the National Research Act (Pub. L. 93-348) extended only until the Commission had submitted its Recommendations to the Secretary on May 21, 1975.

Over 125 individuals commented on subpart C (here stated as subpart B) of the proposed rulemaking which pertains to the fetus, the abortus, the pregnant woman, and the products of human *in vitro* fertilization. Those comments, and the Recommendations of the Commission, are summarized as follows:

Applicability. Commenters objected to the applicability of this subpart to "activities involving women who could become pregnant, except where the applicant or offeror shows to the satisfaction of the Secretary that adequate steps will be taken to avoid involvement of women who are pregnant." Concern was expressed that implementation of such a provisions might involve numerous pregnancy tests during the course of an investigation, and still not achieve this goal. The Department notes that although the Commission expressed concern that the fetus not be involved unintentionally in research activities, it did not make a specific recommendation with respect to this. The Department concludes that the Institutional Review Boards should determine whether adequate measures will be taken to avoid unintentional involvement of pregnant women in research activities which are not designed to include pregnant women or the fetus and which might present a risk to a fetus if such existed. Section 46.102(b)(5) of subpart A is therefore amended to add such determinations as one of the duties of the Institutional Review Board.

The notice published August 23, 1974, was limited to biomedical research. That limitation has been removed because, while the Department believes that this subpart applies primarily to biomedical research, other research may be proposed which might fall under the scope of this subpart.

Definitions. The Department has reviewed with care the definitions adopted by the Commission, and determined that those definitions should be incorporated substantially as drafted into the regulations. It should be noted that in so doing, the Department has extended the meaning of the term "fetus" to include the fetus *ex utero* until such time as such a fetus is determined to be viable. The effect of this change is to delete the term "abortus" which appeared in the proposed rulemaking, and refer instead to a fetus *ex utero*. The Department agrees with the Commission that such usage serves the interests of both consistency and clarity, although it may vary at times from legal, medical, or common usage. Also, consistent with the determination discussed above, the definition of "biomedical research" has been dropped.

Ethical advisory boards. A number of respondents expressed concern that an Ethical Advisory Board, as proposed, would be overburdened and would add an unnecessary layer to a review process which is already time consuming. It was also suggested that the Institutional Review Boards can, and in many instances already do, perform at the local level many of the tasks suggested for the Board. On the other hand, some respondents endorsed the proposal as a welcome measure to insure that projects would be stringently reviewed at a national level for ethical considerations prior to receiving support with public monies.

The Commission recommended that a national review body (similar to that proposed by the Department) consider the ethical problems raised by research proposals to which the application of standards enumerated in their recommendations proves difficult.

The Department has considered these suggestions and agrees that whereas the Institutional Review Boards may be able to assume a large share of the ethical review of proposals, it is also true that there will be instances in which the application of standards to specific cases will be difficult or in which review at the national level is desirable. The Department therefore has determined that such an Ethical Advisory Board is necessary to assure that projects supported or conducted by the Department meet ethical standards acceptable to the general community. However, because the nature of the activities may be different and the number of activities requiring review may be large, one Board will be established to provide advice to the Public Health Service and one Board will be established to provide advice to other components of the Department, with respect to policy governing certain kinds of research, and also with respect to the funding of individual proposals which raise ethical problems. While the Boards will propose to the Secretary categories of research which the Board believes either require or do not require their review, research protocols and procedures which involve minimal or no risk, and which clearly conform to the requirements of this subpart, generally need not be reviewed by the Ethical Advisory Board. Research proposals which are judged by agency advisors or staff to require further evaluation of risk or the interpretation of the requirements the Secretary unless the Ethical Advisory Board, or which raise ethical problems, may not be conducted or supported by the Secretary unless the Ethical Advisory Board has reviewed and rendered its advice concerning the research activity. It is intended, ultimately, that a similar requirement for Board review be extended to other classes of research subjects.

A number of comments were received regarding the composition of the Ethical Advisory Board, its duties, or the manner in which it should conduct its meetings. Specifically, the Commission recommended that women and minorities be adequately represented on the Board, and that its deliberations be conducted with full public participation. Many of the suggestions are currently incorporated in regulations governing Federal committee membership and activities. Others will be addressed in the Charter of the Board which the Secre-

[1] These were readopted with minor technical amendments in the FEDERAL REGISTER for March 13, 1975 (40 FR 11854).

tary will publish in the FEDERAL REGISTER at a later date.

Establishment of a consent committee. Although there was general agreement among commenters that provisions should be made to monitor conditions surrounding the consent process, there was criticism of the proposal to create separate committees to perform this function. For the most part, it was felt that the Institutional Review Boards could and should perform this function as part of continuing responsibility for the protection of human subjects. It was further suggested that additional panels should not be created unless the Department has evidence that the necessary functions could not be performed by the Institutional Review Boards or other existing committees.

The Commission noted that it will be undertaking a study, as part of its mandate under Pub. L. 93-348, of the effectiveness of Institutional Review Boards in implementing DHEW regulations for the protection of human subjects. It recommended that until the study is completed, the responsibility for monitoring the consent process should be assumed by the Institutional Review Boards. The Department agrees. The provisions for creating Consent Committees have therefore been deleted, and the duties delegated to them in the proposed rulemaking have been given to the Institutional Review Boards. This is reflected in § 46.205, titled "Additional duties of the Institutional Review Boards in connection with activities involving fetuses, pregnant women, or human *in vitro* fertilization."

The Department received a number of criticisms regarding the provision that the Consent Committee be authorized to terminate the participation of subjects without their consent (§ 46.305(a)(2) of the proposed rulemaking). It was argued that this would be an unwarranted infringement of an individual's right to consent. The Department agrees, and such authority has been deleted.

Research involving in vitro fertilization. Commenters generally endorsed the Department's proposal not to regulate research involving human *in vitro* fertilization other than to require that all proposals involving such research be reviewed for approval by the Ethical Advisory Board. The Commission did not make any recommendation concerning this category of research in the report submitted on May 21. The Department therefore makes no change from the proposed rulemaking with respect to research involving *in vitro* fertilization. The requirement that all such proposals be reviewed by the Ethical Advisory Board, as well as by the Institutional Review Board, appears in §§ 46.204(c) and 46.205 respectively.

Because biomedical research is not yet near the point of being able to maintain for a substantial period the non-implanted product of *in vitro* fertilization, these regulations do not address this point. Given the state of the research, we believe that regulations would be premature. However, the Department anticipates that such a regulation will be prepared when the state of biomedical science so warrants.

Activities involving fetuses in utero or pregnant women. A number of commenters suggested that the rulemaking, as proposed, would hamper research necessary to meet the health needs of pregnant women, fetuses, and neonates. The most frequent references were to studies on placental transfer, the normal course of pregnancy, and the delivery process. Some individuals objected to the prohibition of research prior to the commencement of a procedure to terminate pregnancy, while others objected to any conduct of research even during the process of abortion.

The Commission, in its Recommendations, separated that category of research directed toward the pregnant woman from that directed toward the fetus *in utero*. It further distinguished between therapeutic research and nontherapeutic research, finding therapeutic research to be generally acceptable and desirable, whether directed toward the fetus or the pregnant woman, provided certain specified preconditions are met. The Department agrees that it is useful to distinguish between the fetus *in utero* and the pregnant woman as the primary subject of a research activity and also that research directed at meeting the health needs of the subject is generally acceptable provided certain conditions are met. The regulations therefore address these topics in separate sections.

A. *General limitations.* There were no substantive objections to the intent of restrictions which appeared in various parts of the proposed rulemaking pertaining to: (1) the necessary completion of appropriate animal studies; or (2) the separation of research personnel from decisions regarding the timing or method of terminating pregnancy or regarding the viability of a delivered fetus. Some commenters, and the Commission, recommended the addition of appropriate studies on nonpregnant humans as a prerequisite for research activities covered by this subpart. The Commission further recommended that there should be no significant changes introduced into a delivery procedure solely in the interests of research. The Department has incorporated these provisions in a section titled "General limitations" (§ 46.206) which governs all research activities covered by this subpart.

B. *Activities directed toward pregnant women as subjects.* As noted above, there was little objection from commenters on from the Commission regarding research directed toward the health needs of the pregnant woman. In fact, some respondents urged that care be taken not to infringe the woman's right to privacy and her access to health care. With respect to women's rights, a number of individuals objected to the provision requiring consent other than that of the pregnant woman for research directed toward the health needs of the pregnant woman, and some objected to such consent provisions even when the woman would be participating in nontherapeutic research activities.

The Commission considered that the woman's right to health care is preeminent, and recommended essentially no restrictions on research directed toward the health care of the pregnant woman, so long as the risks to her fetus are minimized as much as possible consistent with meeting her health needs, and provided that she is fully advised of the risks to herself and her fetus. In addition, the general provisions for prerequisite research and for adequate review and supervision of the consent process should be met. The Department agrees.

With respect to research directed toward the pregnant woman but which is not directed toward her health care, there seems to be general agreement that such research should be permitted only if it imposes minimal or no risk to the fetus. There is disagreement among the commenters with respect to paternal consent for this category of research. The Department has considered with care the various arguments with respect to consent other than the pregnant woman's for nontherapeutic research involving the pregnant woman, and concludes that such consent should be obtained except where such research involves the health needs of the woman.

In general, women who are victims of rape are not appropriate subjects for nontherapeutic research. There are some instances, however, in which their participation may be sought (as in studies concerning the effects of rape.) Consent other than hers is not necessary in such cases.

It should be noted in this regard that the Commission, in a number of instances, recommended that research be permitted if the mother has consented and the father has not objected. The Department has concluded that implementation of a provision for absence of objection might present serious problems. Since the absence of objection can best be verified by requesting consent, the Department has retained the requirement for paternal consent when the father's identity and whereabouts can reasonably be ascertained, and if he is reasonably available.

C. *Activities directed towards fetuses in utero as subjects.* No comments were received which expressed objections to the conduct of research activities directed toward the health care of the fetus *in utero*. Rather, the Department was urged not to restrict, and even to encourage, such research.

On the other hand, there was considerable division of opinion regarding research directed toward the fetus which is not related to its health care. Concern was expressed that the fetus might be used as an experimental "object," in a manner inconsistent with its human genetic heritage. This is particularly true when termination of pregnancy is a factor in the research, as in protocols designed to determine the effect on the fetus of drugs administered to a pregnant woman. Questions were raised regarding the ethical validity of consent by a pregnant woman on behalf of a fetus, for its inclusion in a research activity of no benefit to that fetus, especially if the

woman has already decided to terminate her pregnancy.

The Department is sensitive to these concerns. It has reviewed the Recommendations of the Commission regarding this category of research, and is persuaded that those recommendations are sound; namely, that no research be conducted or supported which fails to treat the fetus with proper care and dignity. In addition, the Department agrees that a pregnant woman need not be presumed to lack interest in her fetus even when she has decided to terminate her pregnancy; thus, she may validly be asked for consent for research involving the fetus.

The Department notes that the Commission was created to represent the best judgment of the community, and to make recommendations following an intensive study of the issues. All of the arguments which were submitted to the Department were considered by the Commission in its deliberations, and it is therefore reasonable to accept the findings of the Commission as the best possible judgment on the matter. The Department concludes that the Recommendations of the Commission with respect to research involving the fetus *in utero* should be adopted. These are incorporated in the regulations in § 46.208, with modifications, as noted above, in the provisions for paternal consent.

Activities directed toward fetuses ex utero as subjects. Although some commenters suggested that no research be permitted on the fetus *ex utero*, others were concerned that the proposed rulemaking was too restrictive, and would preclude the development of technology for sustaining premature infants. The Commission recommended that no procedures be applied to a nonviable fetus *ex utero* which would alter its duration of life. It further recommended that if the fetus might possibly be viable, but has not yet been determined to be so, no additional risk to the well-being of that fetus should be imposed by research. It is expected that no procedures will be undertaken which fail to treat the fetus with due care and dignity, or which affront community sensibilities. Further, it is required that if a delivered fetus is determined to be viable, it will be treated as a premature infant, and may be included in research activities according to the regulations to be proposed governing the participation of children in research.

For the reasons stated above, the Department has concluded that the Recommendations of the Commission regarding research on the fetus *ex utero* should be adopted, for the most part. These are incorporated in § 46.209 of the regulations with modifications, as noted above, in the provisions for paternal consent. However, the Secretary is persuaded by the weight of scientific evidence that research performed on the nonviable fetus *ex utero* has contributed substantially to the ability of physicians to bring to viability increasingly small fetuses. The Secretary perceives that it is in the public interest to continue this successful research and accordingly an exception is made to the Recommendations of the Commission to permit research to develop new methods for enabling fetuses to survive to the point of viability.

Activities involving the dead fetus, fetal material, or the placenta. The Department notes, as did the Commission, that research involving the dead fetus and fetal material is governed in part by the Uniform Anatomical Gift Act which has been adopted by 49 States, the District of Columbia and Puerto Rico. There were no substantive recommendations concerning this section, and the regulation therefore differs from the proposed rulemaking only with respect to minor additions for clarification. Any applicable State or local laws regarding such activities are, of course, controlling.

Activities to be performed outside the United States. Consistent with the Commission's Recommendations, § 46.210 of the proposed rulemaking has been deleted, thereby making these regulations applicable to all research conducted or supported by the Department within the United States or abroad.

Modification or waiver of specific requirements. Recognizing the difficulty of applying a specific set of regulations to all situations that may arise in the future, the Department has elected to provide a mechanism for waiver or modification of specific provisions under certain circumstances. Requests from an applicant or offeror for such a waiver or modification must be reviewed by the appropriate Ethical Advisory Board, which after opportunity for public input, shall advise the Secretary as to whether or not the request should be approved. These Boards will conform to the operating procedures required by the Federal Advisory Committee Act.

Activities conducted by departmental employees. In order to make it clear that the requirements of these regulations (Part 46) apply to activities conducted by its own employees, the Department is adding subpart C titled "Activities Conducted by Departmental Employees" as § 46.301.

The moratorium on fetal research imposed on August 27, 1974, is hereby lifted, but such research will be conducted or supported by the Department only in accordance with the following regulations.

Written comments concerning the Recommendations of the Commission may be sent to the Office of Protection from Research Risks, National Institutes of Health, 9000 Rockville Pike, Bethesda, Maryland 20014. All comments received will be available for inspection at the National Institutes of Health, Room 303, Westwood Building, 5333 Westbard Avenue, Bethesda, Maryland, weekdays (Federal holidays excepted) between the hours of 9 a.m. and 4:30.

These regulations shall become effective on August 8, 1975.

Date: July 17, 1975.

THEODORE COOPER,
Assistant Secretary for Health.

Approved: July 29, 1975.

CASPAR W. WEINBERGER,
Secretary.

Accordingly Part 46 of 45 CFR Subtitle A is amended by:

§§ 46.101–46.122 [Redesignated]

1. Designating §§ 46.1 through 46.22 as Subpart A, renumbering these as §§ 46.101 through 46.122, and modifying all references thereto accordingly.

§ 46.102 [Amended]

2. Adding the word "and" at the end of § 46.102(b)(2), changing the semicolon at the end of § 46.102(b)(3) to a period, and deleting § 46.102(b)(4).

3. Redesignating § 46.102(c) as § 46.102(e) and inserting the following new §§ 46.102(c) and 46.102(d):

§ 46.102 Policy.

* * * * *

(c) Unless the activity is covered by Subpart B of this Part, if it involves as subjects women who could become pregnant, the Board shall also determine as part of its review that adequate steps will be taken in the conduct of the activity to avoid involvement of women who are in fact pregnant, when such activity would involve risk to a fetus.

(d) Where the Board finds risk is involved under paragraph (b) of this section, it shall review the conduct of the activity at timely intervals.

* * * *

4. Adding the following new Subpart B and C.

Subpart B—Additional Protections Pertaining to Research, Development, and Related Activities Involving Fetuses, Pregnant Women, and Human In Vitro Fertilization

Sec.

Subpart C—General Provisions

Sec.

AUTHORITY: 5 U.S.C. 301.

Subpart B—Additional Protections Pertaining to Research, Development, and Related Activities Involving Fetuses, Pregnant Women, and Human In Vitro Fertilization

§ 46.201 Applicability.

(a) The regulations in this subpart are applicable to all Department of Health, Education, and Welfare grants and contracts supporting research, development, and related activities involving: (1) The fetus, (2) pregnant women, and (3) human *in vitro* fertilization.

(b) Nothing in this subpart shall be construed as indicating that compliance

with the procedures set forth herein will in any way render inapplicable pertinent State or local laws bearing upon activities covered by this subpart.

(c) The requirements of this subpart are in addition to those imposed under the other subparts of this part.

§ 46.202 Purpose.

It is the purpose of this subpart to provide additional safeguards in reviewing activities to which this subpart is applicable to assure that they conform to appropriate ethical standards and relate to important societal needs.

§ 46.203 Definitions.

As used in this subpart:

(a) "Secretary" means the Secretary of Health, Education, and Welfare and any other officer or employee of the Department of Health, Education, and Welfare to whom authority has been delegated.

(b) "Pregnancy" encompasses the period of time from confirmation of implantation until expulsion or extraction of the fetus.

(c) "Fetus" means the product of conception from the time of implantation until a determination is made, following expulsion or extraction of the fetus, that it is viable.

(d) "Viable" as it pertains to the fetus means being able, after either spontaneous or induced delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heart beat and respiration. The Secretary may from time to time, taking into account medical advances, publish in the FEDERAL REGISTER guidelines to assist in determining whether a fetus is viable for purposes of this subpart. If a fetus is viable after delivery, it is a premature infant.

(e) "Nonviable fetus" means a fetus *ex utero* which, although living, is not viable.

(f) "Dead fetus" means a fetus *ex utero* which exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord (if still attached).

(g) "*In vitro* fertilization" means any fertilization of human ova which occurs outside the body of a female, either through admixture of donor human sperm and ova or by any other means.

§ 46.204 Ethical Advisory Boards.

(a) Two Ethical Advisory Boards shall be established by the Secretary. Members of these Boards shall be so selected that the Boards will be competent to deal with medical, legal, social, ethical, and related issues and may include, for example, research scientists, physicians, psychologists, sociologists, educators, lawyers, and ethicists, as well as representatives of the general public. No board member may be a regular, full-time employee of the Federal Government.

(b) One Board shall be advisory to the Public Health Service and its components. One Board shall be advisory to all other agencies and components within the Department of Health, Education, and Welfare.

(c) At the request of the Secretary, the appropriate Ethical Advisory Board shall render advice consistent with the policies and requirements of this Part as to ethical issues, involving activities covered by this subpart, raised by individual applications or proposals. In addition, upon request by the Secretary, the appropriate Board shall render advice as to classes of applications or proposals and general policies, guidelines, and procedures.

(d) A Board may establish, with the approval of the Secretary, classes of applications or proposals which: (1) Must be submitted to the Board, or (2) need not be submitted to the Board. Where the Board so establishes a class of applications or proposals which must be submitted, no application or proposal within the class may be funded by the Department or any component thereof until the application or proposal has been reviewed by the Board and the Board has rendered advice as to its acceptability from an ethical standpoint.

(e) No application or proposal involving human *in vitro* fertilization may be funded by the Department or any component thereof until the application or proposal has been reviewed by the Ethical Advisory Board and the Board has rendered advice as to its acceptability from an ethical standpoint.

§ 46.205 Additional duties of the Institutional Review Boards in connection with activities involving fetuses, pregnant women, or human in vitro fertilization.

(a) In addition to the responsibilities prescribed for Institutional Review Boards under Subpart A of this part, the applicant's or offeror's Board shall, with respect to activities covered by this subpart, carry out the following additional duties:

(1) Determine that all aspects of the activity meet the requirements of this subpart;

(2) Determine that adequate consideration has been given to the manner in which potential subjects will be selected, and adequate provision has been made by the applicant or offeror for monitoring the actual informed consent process (e.g., through such mechanisms, when appropriate, as participation by the Institutional Review Board or subject advocates in: (i) Overseeing the actual process by which individual consents required by this subpart are secured either by approving induction of each individual into the activity or verifying, perhaps through sampling, that approved procedures for induction of individuals into the activity are being followed, and (ii) monitoring the progress of the activity and intervening as necessary through such steps as visits to the activity site and continuing evaluation to determine if any unanticipated risks have arisen);

(3) Carry out such other responsibilities as may be assigned by the Secretary.

(b) No award may be issued until the applicant or offeror has certified to the Secretary that the Institutional Review Board has made the determinations required under paragraph (a) of this section and the Secretary has approved these determinations, as provided in § 46.115 of Subpart A of this part.

(c) Applicants or offerors seeking support for activities covered by this subpart must provide for the designation of an Institutional Review Board, subject to approval by the Secretary, where no such Board has been established under Subpart A of this part.

§ 46.206 General limitations.

(a) No activity to which this subpart is applicable may be undertaken unless:

(1) Appropriate studies on animals and nonpregnant individuals have been completed;

(2) Except where the purpose of the activity is to meet the health needs of the particular fetus, the risk to the fetus is minimal and, in all cases, is the least possible risk for achieving the objectives of the activity;

(3) Individuals engaged in the activity will have no part in: (i) Any decisions as to the timing, method, and procedures used to terminate the pregnancy, and (ii) determining the viability of the fetus at the termination of the pregnancy; and

(4) No procedural changes which may cause greater than minimal risk to the fetus or the pregnant woman will be introduced into the procedure for terminating the pregnancy solely in the interest of the activity.

(b) No inducements, monetary or otherwise, may be offered to terminate pregnancy for purposes of the activity.

§ 46.207 Activities directed toward pregnant women as subjects.

(a) No pregnant woman may be involved as a subject in an activity covered by this subpart unless: (1) The purpose of the activity is to meet the health needs of the mother and the fetus will be placed at risk only to the minimum extent necessary to meet such needs, or (2) the risk to the fetus is minimal.

(b) An activity permitted under paragraph (a) of this section may be conducted only if the mother and father are legally competent and have given their informed consent after having been fully informed regarding possible impact on the fetus, except that the father's informed consent need not be secured if: (1) The purpose of the activity is to meet the health needs of the mother; (2) his identity or whereabouts cannot reasonably be ascertained; (3) he is not reasonably available; or (4) the pregnancy resulted from rape.

§ 46.208 Activities directed toward fetuses in utero as subjects.

(a) No fetus *in utero* may be involved as a subject in any activity covered by this subpart unless: (1) The purpose of the activity is to meet the health needs of the particular fetus and the fetus will be placed at risk only to the minimum extent necessary to meet such needs, or (2) the risk to the fetus imposed by the re-

search is minimal and the purpose of the activity is the development of important biomedical knowledge which cannot be obtained by other means.

(b) An activity permitted under paragraph (a) of this section may be conducted only if the mother and father are legally competent and have given their informed consent, except that the father's consent need not be secured if: (1) His identity or whereabouts cannot reasonably be ascertained, (2) he is not reasonably available, or (3) the pregnancy resulted from rape.

§ 46.209 Activities directed toward fetuses ex utero, including nonviable fetuses, as subjects.

(a) No fetus *ex utero* may be involved as a subject in an activity covered by this subpart until it has been ascertained whether the particular fetus is viable, unless: (1) There will be no added risk to the fetus resulting from the activity, and (2) the purpose of the activity is the development of important biomedical knowledge which cannot be obtained by other means.

(b) No nonviable fetus may be involved as a subject in an activity covered by this subpart unless: (1) Vital functions of the fetus will not be artificially maintained except where the purpose of the activity is to develop new methods for enabling fetuses to survive to the point of viability, (2) experimental activities which of themselves would terminate the heartbeat or respiration of the fetus will not be employed, and (3) the purpose of the activity is the development of important biomedical knowledge which cannot be obtained by other means.

(c) In the event the fetus *ex utero* is found to be viable, it may be included as a subject in the activity only to the extent permitted by and in accordance with the requirements of other subparts of this part.

(d) An activity permitted under paragraph (a) or (b) of this section may be conducted only if the mother and father are legally competent and have given their informed consent, except that the father's informed consent need not be secured if: (1) his identity or whereabouts cannot reasonably be ascertained, (2) he is not reasonably available, or (3) the pregnancy resulted from rape.

§ 46.210 Activities involving the dead fetus, fetal material, or the placenta.

Activities involving the dead fetus, mascerated fetal material, or cells, tissue, or organs excised from a dead fetus shall be conducted only in accordance with any applicable State or local laws regarding such activities.

§ 46.211 Modification or waiver of specific requirements.

Upon the request of an applicant or offeror (with the approval of its Institutional Review Board), the Secretary may modify or waive specific requirements of this subpart, with the approval of the Ethical Advisory Board after such opportunity for public comment as the Ethical Advisory Board considers appropriate in the particular instance. In making such decisions, the Secretary will consider whether the risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant such modification or waiver and that such benefits cannot be gained except through a modification or waiver. Any such modifications or waivers will be published as notices in the FEDERAL REGISTER.

Subpart C—General Provisions

§ 46.301 Activities conducted by Department employees.

The regulations of this part are applicable as well to all research, development, and related activities conducted by employees of the Department of Health, Education, and Welfare, except that each Principal Operating Component head may adopt such non-substantive procedural modifications as may be appropriate from an administrative standpoint.

THE NATIONAL COMMISSION FOR THE PROTECTION OF HUMAN SUBJECTS OF BIOMEDICAL AND BEHAVIORAL RESEARCH

RESEARCH ON THE FETUS

Report and Recommendations

MAY 21, 1975.

CONTENTS

I. THE MANDATE

The National Research Act (Pub. L. 93-348) established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research and gave the Commission a mandate to investigate and study research involving the living fetus, and to recommend whether and under what circumstances such research should be conducted or supported by the Department of Health, Education, and Welfare. A deadline of four months after the members of the Commission took office was imposed for the Commission to conduct its study and make recommendations to the Secretary, DHEW. The priority assigned by Congress to research involving the fetus indicates the concern that unconscionable acts involving the fetus may have been performed in the name of scientific inquiry, with only proxy consent on behalf of the fetus.

The members of the Commission determined at the outset to undertake a careful study of the nature and extent of research on the fetus, the range of views on the ethical acceptability of such research, and the legal issues involved, prior to formulating their recommendations. To this end, the Commission has accumulated an extensive body of information, held public hearings, questioned a panel of distinguished ethicists, and conducted lengthy deliberations. In the course of these activities, the Commission has given close scrutiny to many important questions that surround research on the fetus, for example: What are the purposes of research on the fetus? What procedures have been employed in such research? Are there alternatives to such research? Can appropriate consent to such research be obtained by proxy? Under what conditions may research be done on a fetus that is to be aborted, or a nonviable delivered fetus? What review of proposed research should be required?

In the remainder of Section I, the background and activities of the Commission are summarized, and the definitions used in this report are set forth. Reports, papers and testimony that were prepared for or presented to the Commission are summarized in Sections II

REVIEW OF THE USE OF HUMAN SUBJECTS: INSTRUCTIONS FOR INVESTIGATORS

Appendix E. Review of the Use of Human Subjects: Instructions for Investigators

Who needs to seek review?

Any individual who is responsible for an activity involving human subjects conducted at or sponsored by the University of Illinois - Urbana-Champaign.

What kinds of activity require review?

Any activity involving human subjects, i.e., human beings whose physical, emotional or behavioral condition, responses, tissues or fluids are investigated for any purpose other than for the sole purpose of benefitting the subject as an individual. The use of interviews, tests, observations and inquiries designed to elicit non-public information about individuals or groups must be reviewed. Routine course development, including evaluation of the effectiveness of such development, in courses sponsored by UIUC do not need review. Nor do non-intervening observation of public behavior, secondary use of data if the subjects are not identifiable, and use of publicly available data whether or not the subjects are identifiable.

Research projects, demonstration activities, pilot projects, student dissertation projects, independent study projects, course projects must be reviewed if they involve human subjects.

What is meant by the terms subject, research, "at risk", informed consent?

See Part II, pages 5-13, of The Use of Human Subjects in Research at the University of Illinois - Urbana-Champaign (copies available in departmental offices or from the Executive Secretary of the Institutional Review Board.)

What is the purpose of the review?

The purpose of the review is to obtain an independent determination of whether the human subjects will be placed at risk, and if risk is involved, that

a) any risks to the subject are so outweighed by the sum of the benefit to the subject and importance of the knowledge to be gained as to warrant a decision to allow the project to be undertaken;

b) the welfare of any such subjects will be adequately protected; and

c) legally effective informed consent will be obtained by adequate and appropriate methods.

When must an activity involving human subjects be reviewed?

Prior to initiation of activity, prior to implementation of any changes in procedures involving human subjects, and at least annually during the lifetime of the project. If the project is being proposed for external funding, review should take place prior to submission of proposal to funding agency.

Who will perform the review?

The identity of the reviewers will depend upon the nature of the activity as follows:

Source of funding	Nature of Activity	Reviewer
Not externally funded	Complies with IRB approved departmental guidelines	Department executive office or his designee
	Does not comply with IRB approved departmental guidelines	IRB
	Department does not have IRB approved guidelines	IRB
Externally funded		IRB

What must be submitted to reviewers?

1. Form IRB-1, "Information for Review of Activity involving Human Subjects"

   This form must be submitted for all activities to be reviewed by the IRB. Its use in departmental review of non-externally funded activities falling within IRB approved departmental guidelines is optional. Check with department executive officer.

2. Description of project, its objectives and significance

   If the project is being proposed to an external funding agency, submit a copy of the proposal.

3. Description of method to be used for obtaining subjects and for assuring that their participation is voluntary.

   In the selection of potential subjects, prior professional relationships must be respected. If the study involves patients or clients, then the personal physician or other professional involved must first determine that the patient or client is willing to discuss the study before the investigator can approach the potential subject.

   If physicians or agencies merely provide the investigator with the names of those patients or clients with characteristics that make them eligible as subjects in the study, they are violating their confidential relationships. Investigators should neither request nor accept the names unless they are assured that the patients or clients have agreed to be approached.

4. Description of how subjects will be used, the possible risks to the subject, the potential benefits to the subject and/or to others.

   The material submitted should be brief, concise, but complete. For example, if human blood will be used, identify the donors, how they will be asked to participate, amount of blood to be taken, how it will be taken, by whom, (indicate credentials) how frequently, If drugs are to be administered, indicate identity of drug, whether or not it is FDA certified, dosage, by whom it will be administered, period of administration, anticipated effects.

   If subjects will be interviewed or will be asked to complete questionnaires or take tests, indicate the nature of questions or test material, the degree of confidentiality needed and how it is to be assured.

If any initial deception is involved to avoid invalidation or biasing of the investigation, indicate what information will be withheld, why incomplete disclosure is justified, and describe the debriefing procedure to be used.

If subjects are to receive payment or other incentives for participation, describe such incentives. Note that payment to subjects is considered to be income by the Internal Revenue Service, and must be reported as such.

5. Description of the method to be used for securing legally effective informed consent of subjects who will be placed at risk.

   Note that the signature of a parent or legal guardian is necessary to obtain legally effective informed consent of a subject who is a minor or who is other wise considered legally incompetent.

   Copies of sample consent forms to be used and any written or oral explanation to be given to subjects must be submitted to the IRB for review.

   Note that DHEW has specific requirements regarding the obtaining and documenting of informed consent. See Appendix D, Sections 46.9 and 46.10. Sample consent forms which satisfy these regulations are provided in Appendix A.

6. Description of provisions for safeguarding the rights and welfare of the human subjects to be involved, including the provisions for assuring confidentiality of data and any provision for medical care or supervision.

How will project director find out result of review?

Results of reviews conducted by IRB will be provided to project director by letter from the Executive Secretary of the IRB.

Results of reviews conducted by department executive officers or their designee will be reported in accordance with departmental practice. Check with the department executive officer for further information.

How can a project director obtain information or advice and counsel regarding the use of human subjects?

The investigator may contact the Executive Secretary of the Institutional Review Board who will either provide the information requested or arrange for the investigator to discuss the matter with one or more members of the Institutional Review Board.

Are there special requirements for review of the use of subjects if access to the subjects is gained through cooperating institutions not under the control of the university?

There may be. If the subjects are not at risk, no special documentation is required, but investigators gaining access to subjects in another institution should always assure that the authorized official of the institution is informed of the study.

If the subjects are at risk, the material submitted for IRB review of the project must include the following information.

Status of Subjects: ☐ Wards ☐ Residents ☐ Employees

☐ Patients ☐ Students ☐ Other (explain)

Number of Subjects: _____ Age Range of Subjects: _____

Name & Address of Cooperating Institution _____

_____

_____

_____

Name of Authorizing Official of Cooperating Institution _____

_____

Title of Authorizing Official _____

Official Signature _____

Telephone Number _____

Who is responsible for informed consent documents?

The investigator is responsible for obtaining and storing signed consent documents. These documents should be handled and stored appropriately to protect the identity of the subject. They must be available for IRB inspection upon request. If the investigator leaves the university, the signed consent forms must be turned over to the IRB and must be retained at the University so that it can fulfill its administrative responsibilities.

How long must records on the use of human subjects be retained?

If the project is externally supported, the terms of the grant or contract usually indicate how long records must be retained. Usually a period of five years beyond expiration of the support agreement is sufficient for compliance with the terms of the agreement. Since the Illinois statute of limitations and discovery also apply, it is advisable for the investigator to consult the university's legal counsel before destroying such records. Consent documents and other important records relating to the use of minors who were placed at risk should be retained until at least two years after the minor reaches majority.

For projects which are not externally funded, the IRB recommends retention of documents for five years beyond termination of the project, unless the nature of the project indicates that a longer time would be advisable. Again the Illinois statute of limitations and discovery apply so that advice from legal counsel is appropriate before records are destroyed.

How should emergencies involving human subjects be handled?

The university maintains McKinley Health Center, which includes a hospital having 58 beds, the usual hospital facilities, and a staff of physicians. This facility is available for emergencies that may arise in course of UIUC activities involving human subjects. Arrangements may be made for physicians from McKinley Health Center or from local hospitals to monitor work involving human subjects when the Institutional Review Board finds the element of risk to warrant supervision by medical personnel.

What are the subject's privileges?

If a subject or prospective subject wishes to review the UIUC policies and procedures, he/she may request a copy from the department executive officer or the Executive Secretary of the Institutional Review Board, or may review it in the Reference Room of the University Library. Copies of the UIUC Assurance filed with DHEW are available in the Office of the Executive Secretary of the Institutional Review Board. One copy is on file in the University Library Reference Room.

If a subject wishes to voice complaints or concerns regarding his/her participation in a project, he/she should take the matter to the executive officer* of the department in which the activity is supervised. The subject may, if not satisfied with the results of that process, refer his/her concerns to the Executive Secretary of the Institutional Review Board, who will arrange for the matter to be considered by the Institutional Review Board.

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it executive officers are responsible for notifying the Institutional view Board of any problems which arise involving human subjects.